

DeepMAge: A Methylation Aging Clock Developed with Deep Learning

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Supplementary Materials

Comparing DeepMAge to a de novo linear model

While Horvath's 353 CpG aging clock is a well-known frame of reference for age predictors, it is not sufficient to show the extra benefits offered by deep learning compared to linear machine learning techniques. Horvath's DNAm clock was trained on a different data collection, and the original paper suggests training models from scratch for new datasets.

Thus, to show deep learning superiority relative to other algorithms, we reproduced an elastic net aging clock as described in Horvath's original paper, using the same data as for DeepMAge. The resulting model contains 348 CpGs, 75 of which overlap with the 353 CpGs originally described by Horvath (Supplementary Table 5). We then verified the obtained linear predictor in the verification set containing 1,293 samples and found that both its MAE = 4.24 and MedAE = 3.23 years were higher than those of DeepMAge in the same set (MAE = 3.80, MedAE = 2.77 years). The difference between MAEs, although slight, was deemed significant, with a *p-value* = 0.0001 (Supplementary Fig. 6).

The R script used to reproduce Horvath's method and the corresponding prediction tables can be found in the Supplementary Script section (Supplementary Script 1).

Comparing DeepMAge to the 71 CpG clock

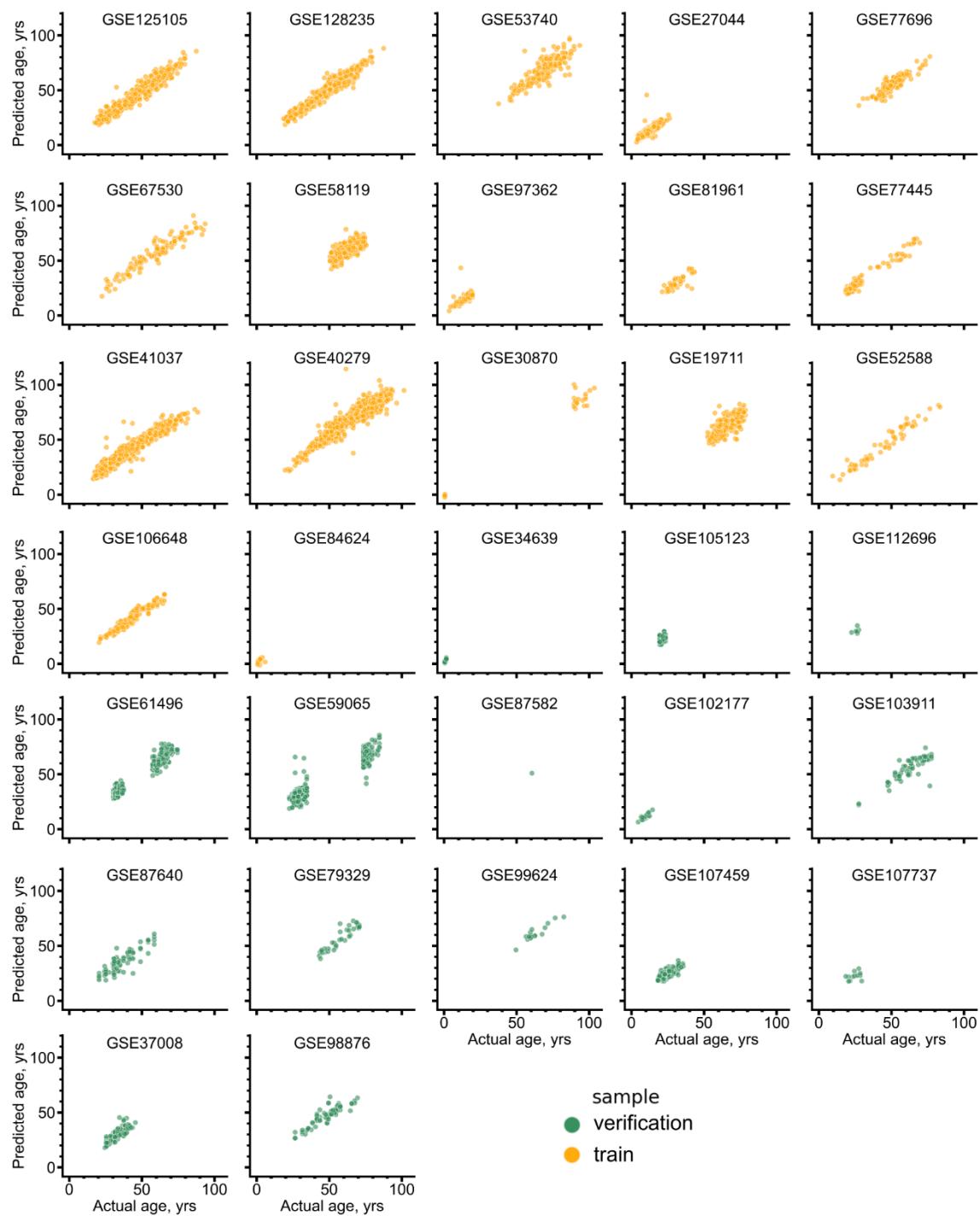
In addition to the 353 CpG clock, we also compared DeepMAge to the 71 CpG and 89 CpG blood DNAm clocks published by Hannum in 2013 [13]. The 71 CpG aging clock was developed using only blood-derived data obtained with the Illumina 450k platform.

We used the coefficients from the original linear regressions and tested these models on studies within the verification set, as defined by the current study. In a set of 1,404 DNAm profiles, both DeepMAge and the 71 CpG clock performed better than the baseline mean age assignment, but DeepMAge showed superior performance in terms of both RMSE and MAE (Supplementary Table 4). The RMSE of the 71 CpG clock (15.12 years) was significantly higher than the accuracy reported in the original paper (3.9 years).

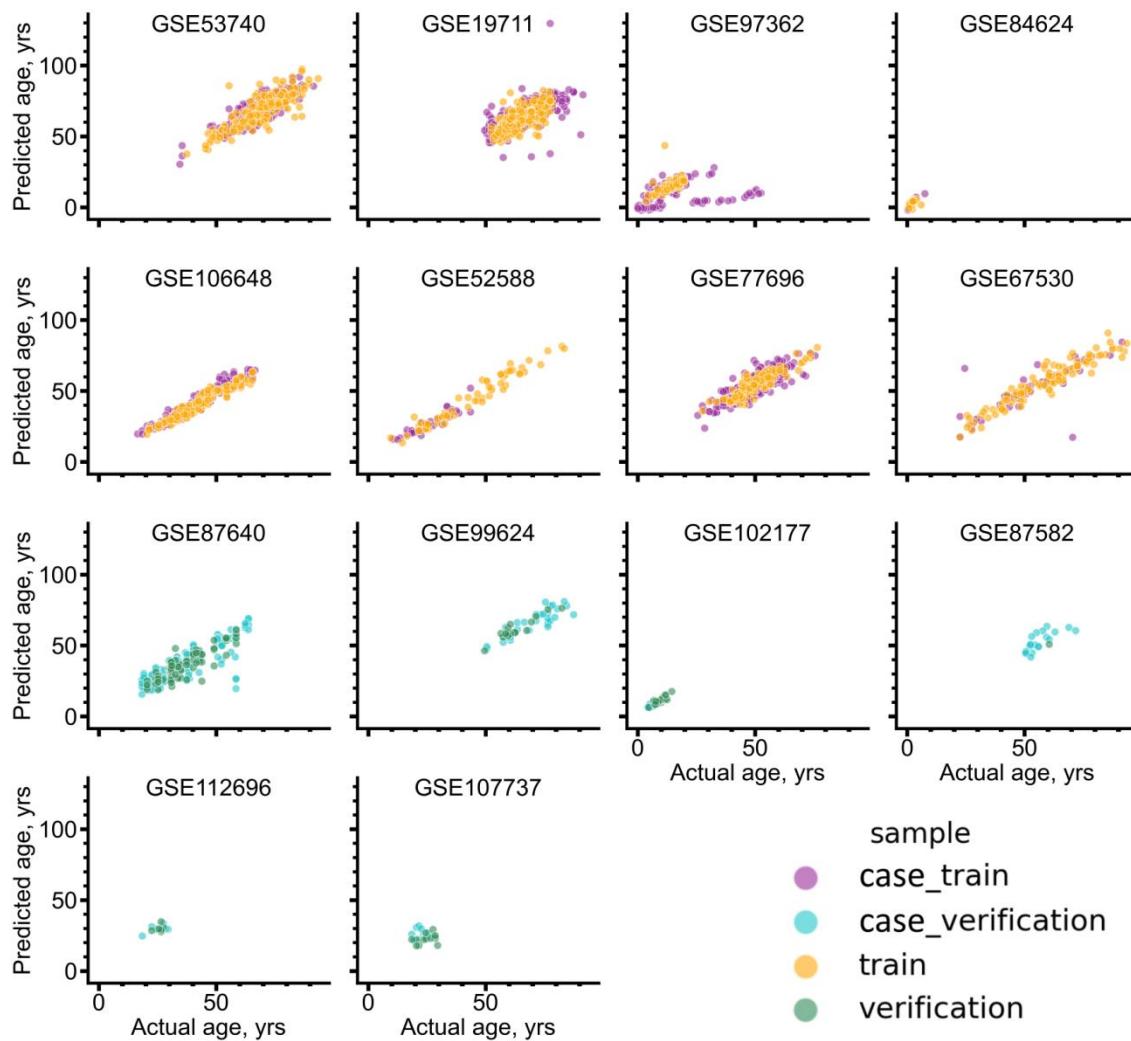
The MedAE achieved by the CpG clock for this set was 7.63 years. The MedAE achieved by DeepMAge for this set was 3.97 years.

The cause of such poor performance of the 71 CpG clock may be its training set size, which contained just 656 individuals. The 353 CpG clock, in turn, was trained on a set containing 7,844 multi-tissue DNAm profiles, and DeepMAge was trained on 4,930 blood samples.

Note: All supplementary tables and the supplementary R script have been uploaded to the Open Science Framework (<https://dx.doi.org/10.17605/OSF.IO/74ZGA>).

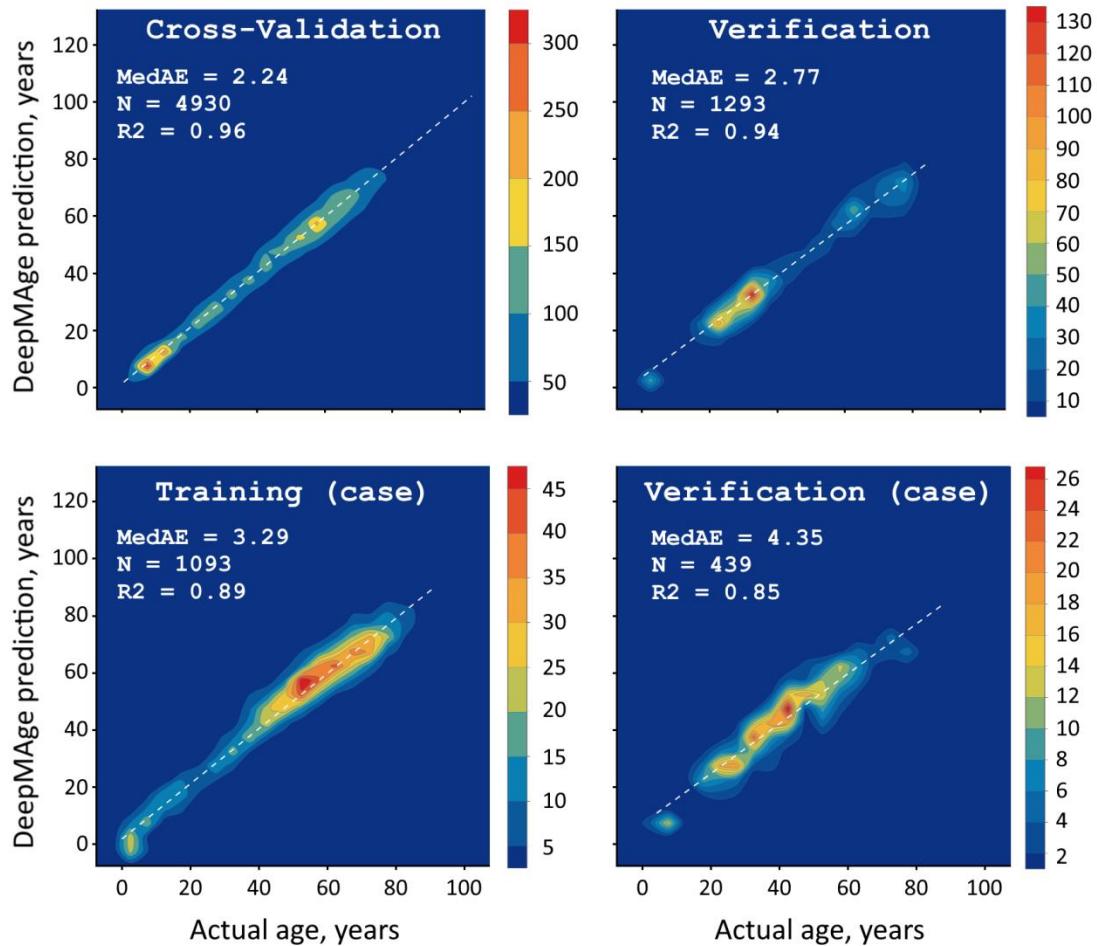


Supplementary Figure 1. DeepMAge accurately predicted the ages of the healthy blood sample donors of all studies from the training and verification sets. Training set predictions were obtained during cross-validation.
Yrs = Years

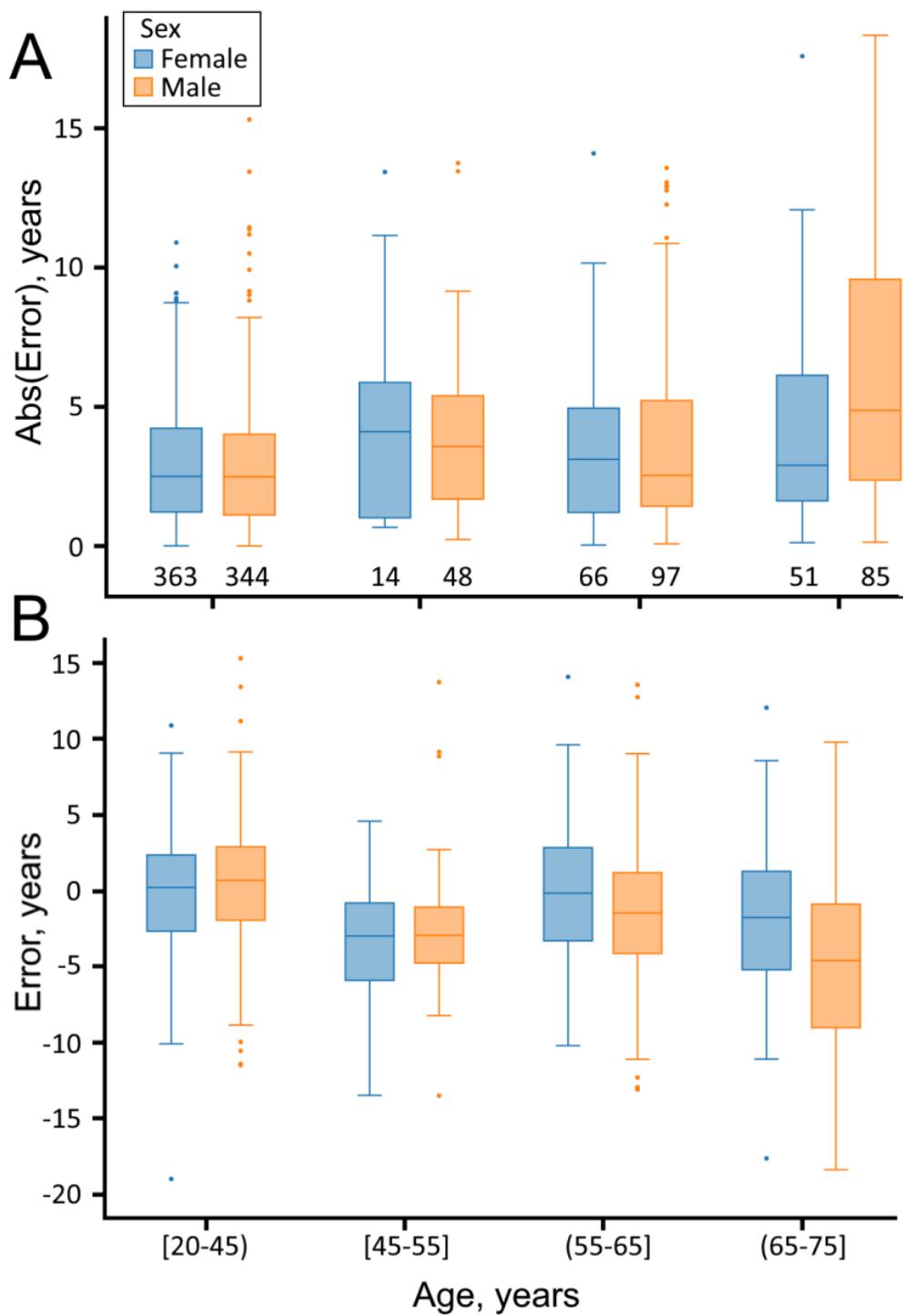


Supplementary Figure 2. DeepMAge accurately predicted the ages of the blood sample donors of the case-control studies from the training and verification sets.

Yrs = Years

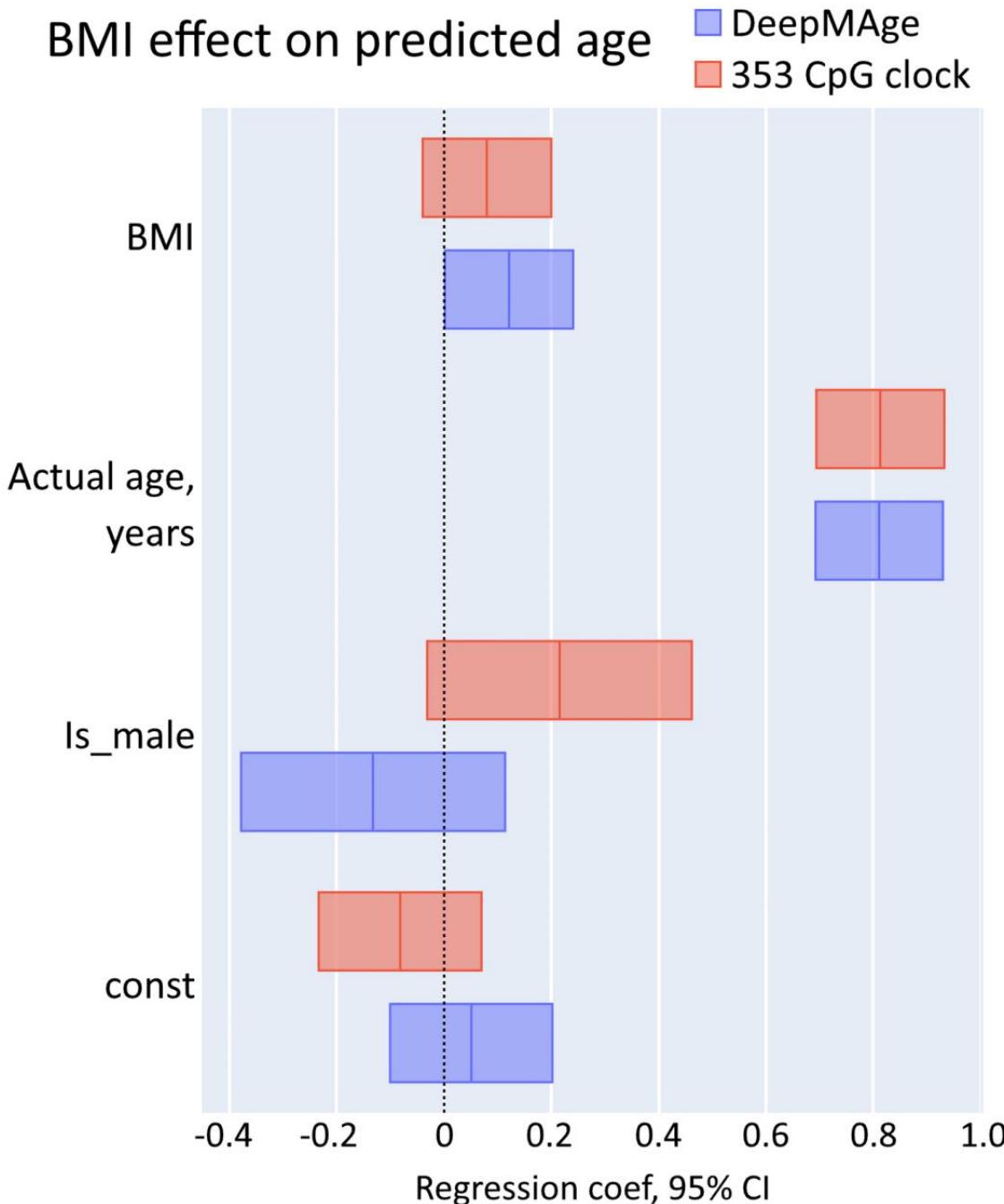


Supplementary Figure 3. KDE representation of Fig.1 in the main text. DeepMAge accurately predicted the chronological ages of both healthy individuals (top) and in an aggregation of case cohorts from multiple studies (bottom). All the cohorts, apart from the “Cross-Validation” cohort, were predicted by the final model. The “Training (case)” cohort refers to the samples that were present in the studies used for training but were excluded from CV because they came from unhealthy donors. Similarly, the “Verification” cohort contains only healthy donors, and the “Verification (case)” cohort contains donors with various health conditions from the same studies. MedAE = Median absolute error measured in years; N = Number of samples in a corresponding cohort; R² = Coefficient of determination. The white dashed lines are the least squares regressions. The number of counts contained within each contour of the 2D histograms is color-coded according to the color bars to the right of each subplot.



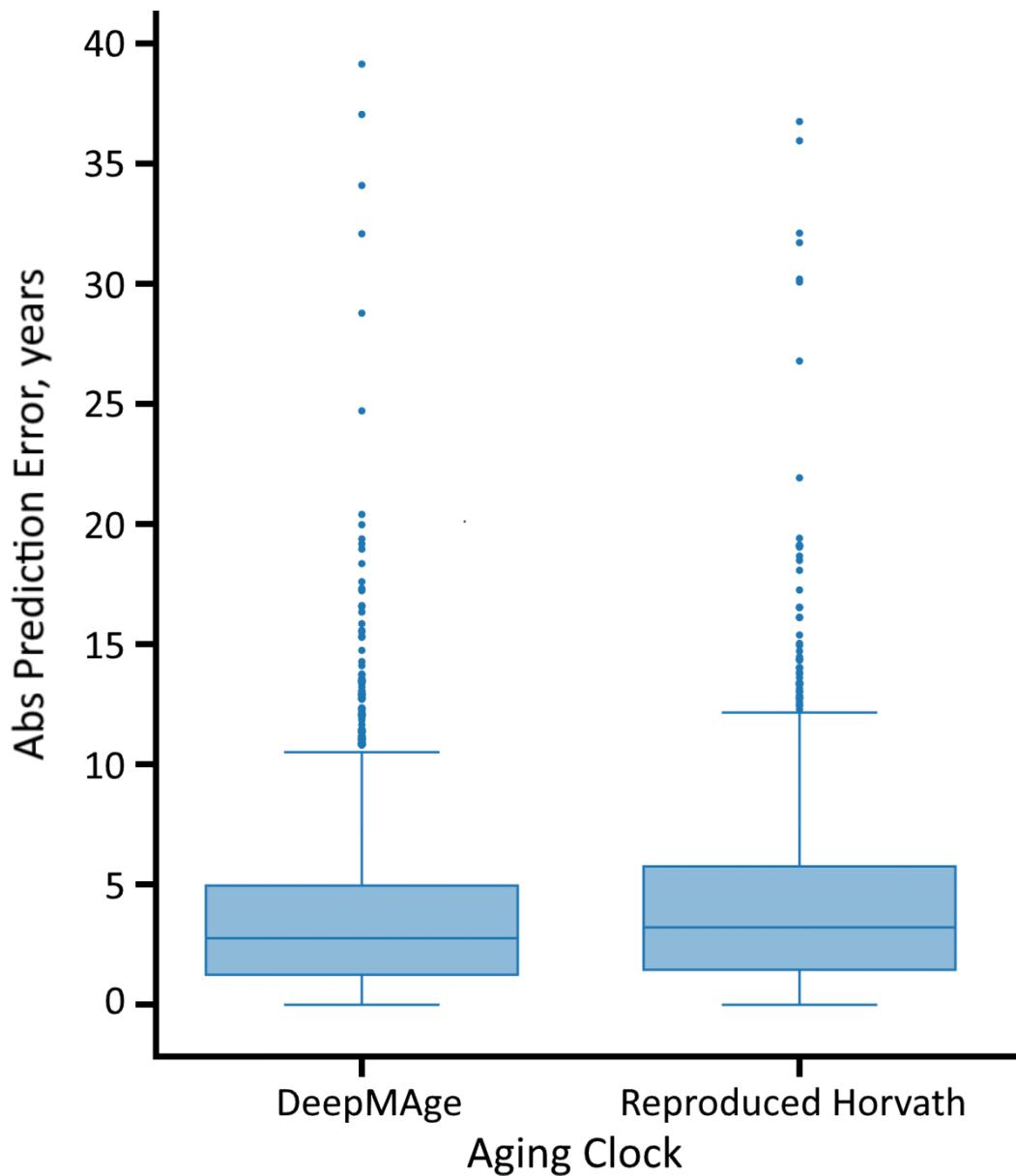
Supplementary Figure 4. Older adults but not younger adults have significantly different DeepMAge error distributions for males and females (Table 2). (A) DeepMAge absolute prediction error per age group in the verification set. The number of samples in each age group is marked below the boxes; (B) DeepMAge prediction error per age group in the verification set; The middle lines represent the medians; the box edges represent the quartiles; the whiskers reach out no farther than 1.5 times the interquartile distance. Four upper outliers in the [20-45] female age group were removed for presentation purposes. Abs (Error) = absolute error

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Supplementary Figure 5. Scaled BMI effect on age prediction, as observed in [Predicted ~ Real Age + Sex + BMI] ordinary least squares linear regression. BMI had a significant effect ($p\text{-value} = 0.048$) on the predicted age for DeepMAge, but not for Horvath's aging clock ($p\text{-value} = 0.19$). Data set used: GSE37008. The middle lines of the boxes represent the point estimate for the regression coefficients; their edges represent the 2.5% and the 97.5% CI borders. BMI = Body mass index; CI = Confidence interval; const = Model intercept

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Supplementary Figure 6. Boxplots for absolute prediction errors in the DeepMAge and the *de novo* elastic net regressor reproduced according to Horvath's protocol. The MAE of DeepMAge (3.80 years) was significantly lower ($p\text{-value} = 0.0001$) than that of the elastic net (4.24 years). The total number of samples used was 1,293. The middle lines represent the medians; the box edges represent the quartiles; the whiskers reach out no farther than 1.5 times the interquartile distance.

Abs = Absolute; MAE = Mean Absolute Error

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Supplementary Table 1. Per-study report containing DeepMAge accuracy (MedAE in years), DeepMAge cohort, male ratio, and age range, as well as the baseline accuracy (median age assignment).

Study	Cohort	N, samples	Male ratio, %	Age range, years	MedAE, years	Baseline, years	Platform
GSE81961	train	40	0.0	21-43	2.62	3.65	450k
GSE52588	train	58	12.0	9-83	2.72	14.0	450k
GSE52588	case_train	29	62.0	10-43	2.82	8.0	450k
GSE97362	train	83	67.0	3-19	1.4	3.0	450k
GSE97362	case_train	150	61.0	0-52	3.47	5.5	450k
GSE41037	train	720	62.0	16-88	2.29	10.0	27k
GSE30870	train	39	0.0	0-103	2.96	14.0	450k
GSE61496	verification	310	53.0	30-74	2.14	16.5	450k
GSE98876	verification	71	100.0	26-69	2.54	6.0	450k
GSE37008	verification	99	37.0	24-45	3.74	4.0	27k
GSE128235	train	536	43.0	18-87	1.99	9.0	450k
GSE87640	case_verification	156	65.0	18-63	3.97	8.8	450k
GSE87640	verification	84	62.0	20-58	2.52	5.05	450k
GSE87582	case_verification	20	90.0	50-71	4.38	2.81	450k
GSE87582	verification	1	100.0	60-60	9.59	0.0	450k
GSE19711	train	272	0.0	52-78	4.25	6.0	27k
GSE19711	case_train	264	0.0	49-91	3.7	8.0	27k
GSE34639	verification	48	33.0	0-1	1.92	0.5	450k
GSE79329	verification	34	100.0	43-70	2.63	8.7	450k
GSE67530	train	105	53.0	22-93	4.43	12.0	450k
GSE67530	case_train	39	59.0	22-91	3.43	10.0	450k
GSE105123	verification	107	58	19-23	2.06	1.0	450k
GSE99624	case_verification	32	12.0	50-87	3.92	7.5	450k
GSE99624	verification	16	38.0	49-82	2.72	2.5	450k
GSE125105	train	688	45.0	17-87	2.1	11.0	450k
GSE102177	case_verification	18	61.0	4-10	1.84	0.53	450k
GSE102177	verification	18	56	4-14	1.87	2.0	450k
GSE20067	case_verification	195	49.0	24-74	4.99	6.0	27k
GSE27044	train	889	100.0	3-26	1.08	3.0	27k
GSE103911	verification	65	71.0	27-77	6.96	8.0	450k
GSE53740	train	197	32.0	37-93	2.95	7.0	450k
GSE53740	case_train	186	35.0	34-91	3.62	4.5	450k
GSE59065	verification	295	48.0	22-84	4.35	11.0	450k
GSE112696	case_verification	6	67.0	18-29	5.51	3.0	450k
GSE112696	verification	6	67.0	22-27	3.75	0.5	450k
GSE77696	train	117	88.0	27-76	4.24	5.0	450k
GSE77696	case_train	261	96.0	25-75	4.25	6.0	450k
GSE58119	train	282	0.0	50-75	3.89	5.0	27k
GSE106648	train	139	25.0	20-65	2.48	7.0	450k
GSE106648	case_train	140	30.0	16-66	1.74	9.0	450k
GSE77445	train	85	51.0	18-69	2.7	4.0	450k
GSE84624	train	24	50.0	0-5	1.32	0.42	450k
GSE84624	case_train	24	54.0	0-7	1.27	0.9	450k
GSE107737	case_verification	12	100.0	18-27	2.46	2.0	450k
GSE107737	verification	12	100.0	18-29	3.03	3.5	450k
GSE40279	train	656	48.0	19-101	4.25	11.0	450k
GSE107459	verification	127	0.0	18-35	1.63	2.72	450k

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Supplementary Table 2. 1,000 CpG sites comprising DeepMAGE, ranked by feature importance (higher importance features come first).

Rank	CpG site	Importance	Rank	CpG site	Importance	Rank	CpG site	Importance	Rank	CpG site	Importance	
1	cg01580	0.000149	31	cg15319	7.45E-05	61	cg08209	6.14E-05	91	cg00462	5.47E-05	
2	888	323	32	cg11668	7.41E-05	62	cg18182	6.13E-05	92	994	5.47E-05	
3	378	596	33	844	7.32E-05	63	cg07388	6.11E-05	93	cg11377	5.45E-05	
4	378	0.000143	34	cg00343	0.000143	64	493	cg17729	6.11E-05	94	136	5.45E-05
5	092	059	35	604	7.21E-05	65	667	cg26372	6.08E-05	95	905	5.44E-05
6	940	94	36	cg27015	7.18E-05	66	517	cg19885	6.05E-05	96	cg25564	5.43E-05
7	906	211	37	931	7.21E-05	67	761	cg26842	5.99E-05	97	800	5.43E-05
8	354	079	38	cg19046	7.18E-05	68	024	cg23303	5.95E-05	98	cg05436	5.42E-05
9	943	798	39	959	7.05E-05	69	867	cg12238	5.95E-05	99	231	5.42E-05
10	407	461	40	cg08668	7.05E-05	70	074	cg24826	5.95E-05	100	cg00987	5.42E-05
11	994	796	41	790	6.88E-05	71	475	cg10362	5.94E-05	101	379	5.42E-05
12	943	0.000107	42	cg15111	6.81E-05	72	964	cg11299	5.92E-05	102	cg01820	5.42E-05
13	407	0.000107	43	cg00503	6.77E-05	73	000	cg22947	5.91E-05	103	374	5.40E-05
14	407	461	44	840	6.77E-05	74	694	cg06268	5.90E-05	104	343	5.39E-05
15	994	796	45	cg20143	6.77E-05	75	344	cg16785	5.88E-05	105	369	5.36E-05
16	943	0.000106	46	cg12373	6.76E-05	76	470	cg19724	5.88E-05	106	cg23887	5.36E-05
17	019	9.53E-05	47	771	6.76E-05	77	694	cg07158	5.84E-05	107	396	5.29E-05
18	887	9.13E-05	48	cg15957	6.76E-05	78	000	cg01530	5.84E-05	108	594	5.29E-05
19	230	9.11E-05	49	394	6.72E-05	79	694	cg03330	5.84E-05	109	cg04662	5.29E-05
20	cg04836	0.000105	50	cg18902	6.72E-05	80	339	cg06268	5.84E-05	110	544	5.27E-05
21	038	8.82E-05	51	090	6.72E-05	81	073	cg26845	5.84E-05	111	cg13931	5.27E-05
22	cg09809	0.000106	52	cg15013	6.70E-05	82	300	cg05822	5.84E-05	112	228	5.26E-05
23	672	8.76E-05	53	019	6.66E-05	83	898	cg21790	5.84E-05	113	228	5.26E-05
24	cg02479	0.000107	54	cg03623	6.66E-05	84	626	cg16744	5.84E-05	114	772	5.25E-05
25	575	8.66E-05	55	019	6.64E-05	85	626	cg18660	5.84E-05	115	544	5.24E-05
26	230	8.63E-05	56	cg02397	6.64E-05	86	898	cg02310	5.84E-05	116	cg06836	5.24E-05
27	847	8.50E-05	57	514	6.57E-05	87	640	cg18440	5.84E-05	117	772	5.24E-05
28	cg27320	0.000107	58	cg15804	6.53E-05	88	048	cg13460	5.84E-05	118	873	5.23E-05
29	127	8.47E-05	59	973	6.53E-05	89	246	cg20300	5.84E-05	119	263	5.23E-05
30	cg05675	0.000107	60	cg16744	6.53E-05	90	322	cg20761	5.84E-05	120	802	5.22E-05
Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	
121	cg0869583	5.01E-05	151	cg1392135	4.67E-05	181	cg02154074	4.40E-05	211	cg07313155	4.21E-05	
122	0	5.00E-05	152	2	4.66E-05	182	cg21448423	4.40E-05	212	cg08186362	4.20E-05	
123	cg0487268	4.98E-05	153	cg2187088	4.65E-05	183	cg09949775	4.39E-05	213	cg130215	4.20E-05	

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124	cg1536159 0	4.98E-05	154	cg0789514 9	4.64E-05	184	cg02840794	4.39E-05	214	cg25141674	4.17E-05
125	cg1520187 7	4.97E-05	155	cg0771520 1	4.64E-05	185	cg21581873	4.39E-05	215	cg16933388	4.17E-05
126	cg1899268 8	4.97E-05	156	cg0129520 3	4.64E-05	186	cg17410236	4.38E-05	216	cg02096633	4.17E-05
127	cg1705132 1	4.95E-05	157	cg1667049 7	4.62E-05	187	cg25332298	4.37E-05	217	cg23843812	4.16E-05
128	cg0366499 2	4.91E-05	158	cg1678645 8	4.62E-05	188	cg00194146	4.37E-05	218	cg17832674	4.15E-05
129	cg0056568 8	4.89E-05	159	cg1312904 6	4.61E-05	189	cg26599006	4.36E-05	219	cg20295671	4.15E-05
130	cg0442562 4	4.87E-05	160	cg2329034 4	4.61E-05	190	cg27316956	4.36E-05	220	cg19423311	4.14E-05
131	cg2125664 9	4.87E-05	161	cg0447483 2	4.59E-05	191	cg05266781	4.36E-05	221	cg23124451	4.13E-05
132	cg0373487 4	4.87E-05	162	cg2239227 6	4.58E-05	192	cg19357849	4.32E-05	222	cg24989962	4.13E-05
133	cg0284454 5	4.87E-05	163	cg1537963 3	4.58E-05	193	cg24871743	4.32E-05	223	cg22809047	4.13E-05
134	cg2012509 1	4.86E-05	164	cg1921180 0	4.57E-05	194	cg23178308	4.31E-05	224	cg04586023	4.13E-05
135	cg1651640 0	4.84E-05	165	cg2069256 9	4.56E-05	195	cg21700166	4.31E-05	225	cg10741760	4.13E-05
136	cg0740845 6	4.83E-05	166	cg2291972 8	4.54E-05	196	cg16168311	4.30E-05	226	cg11065385	4.12E-05
137	cg1214590 7	4.83E-05	167	cg2636966 7	4.51E-05	197	cg17133388	4.30E-05	227	cg03996822	4.11E-05
138	cg1475458 1	4.82E-05	168	cg0938100 0	4.51E-05	198	cg25499099	4.29E-05	228	cg22730004	4.11E-05
139	cg0626349 5	4.81E-05	169	cg0216404 3	4.51E-05	199	cg18693704	4.28E-05	229	cg03336167	4.10E-05
140	cg1240225 1	4.81E-05	170	cg2522917 6	4.51E-05	200	cg06458239	4.28E-05	230	cg07703401	4.08E-05
141	cg0964354 4	4.80E-05	171	cg1383662 2	4.50E-05	201	cg06738602	4.27E-05	231	cg17339202	4.08E-05
142	cg2600508 2	4.80E-05	172	cg1262049 7	4.50E-05	202	cg01777397	4.27E-05	232	cg17497271	4.07E-05
143	cg1673124 0	4.77E-05	173	cg1357327 9	4.49E-05	203	cg03688818	4.26E-05	233	cg01405761	4.05E-05
144	cg2576378 8	4.75E-05	174	cg1794001 6	4.49E-05	204	cg06204948	4.24E-05	234	cg08900043	4.05E-05
145	cg1416600 9	4.75E-05	175	cg2419983 3	4.48E-05	205	cg25985778	4.24E-05	235	cg08529529	4.05E-05
146	cg0215130 1	4.74E-05	176	cg2661080 4	4.47E-05	206	cg02228185	4.24E-05	236	cg17471102	4.04E-05
147	cg1031663 8	4.71E-05	177	cg0427079 9	4.45E-05	207	cg16363586	4.22E-05	237	cg22892904	4.03E-05
148	cg2217182 5	4.71E-05	178	cg2371021 6	4.44E-05	208	cg26151675	4.22E-05	238	cg24968336	3.99E-05
149	cg1719948 9	4.70E-05	179	cg1189692 8	4.43E-05	209	cg23967169	4.22E-05	239	cg00236832	3.98E-05
150	cg2447189 3	4.69E-05	180	Importanc Ran k	4.42E-05	210	cg24921089	4.22E-05	240	cg15898840	3.97E-05
Ran k	CpG site	e	Ran k	CpG site	e	Ran k	CpG site	e	Ran k	CpG site	e
241	cg0399151 4	3.96E-05	271	cg2382859 5	3.75E-05	301	cg21697134	3.58E-05	331	cg15743985	3.44E-05
242	cg2228562 2	3.96E-05	272	cg1459240 6	3.75E-05	302	cg04601137	3.57E-05	332	cg23854009	3.43E-05
243	cg2384350 1	3.94E-05	273	cg1082217 2	3.75E-05	303	cg24169822	3.57E-05	333	cg19008809	3.43E-05
244	cg1137868 5	3.93E-05	274	cg0506467 3	3.75E-05	304	cg27360098	3.56E-05	334	cg23668631	3.42E-05
245	cg1951551 6	3.92E-05	275	cg0955444 3	3.74E-05	305	cg01968178	3.55E-05	335	cg27153400	3.42E-05
246	cg2321124 8	3.92E-05	276	cg0536914 2	3.74E-05	306	cg02217159	3.55E-05	336	cg11946503	3.42E-05
247	cg2318904 0	3.92E-05	277	cg1727406 4	3.73E-05	307	cg13697378	3.55E-05	337	cg00081975	3.41E-05
248	cg0911862 4	3.92E-05	278	cg2351760 5	3.73E-05	308	cg25044651	3.54E-05	338	cg14175438	3.41E-05
249	cg17688525 5	3.91E-05	279	cg2199225 0	3.73E-05	309	cg16319578	3.54E-05	339	cg17688525	3.41E-05

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250	cg0476542 2 cg2691178	3.91E-05	280	cg2097419 6 cg1112055	3.72E-05	310	cg09067967	3.54E-05	340	cg27553955	3.41E-05
251	7 cg1153694	3.91E-05	281	1 cg1191969	3.72E-05	311	cg12688670	3.54E-05	341	cg05767404	3.41E-05
252	0 cg2582270	3.90E-05	282	4 cg1431940	3.69E-05	312	cg03891319	3.53E-05	342	cg27016307	3.40E-05
253	9 cg1445668	3.90E-05	283	9 cg1662003	3.68E-05	313	cg18919097	3.53E-05	343	cg12782180	3.40E-05
254	3 cg1529765	3.89E-05	284	2 cg1978946	3.67E-05	314	cg09736162	3.53E-05	344	cg16465939	3.40E-05
255	0 cg2358744	3.88E-05	285	6 cg2545932	3.67E-05	315	cg14261309	3.53E-05	345	cg03224418	3.40E-05
256	9 cg0588113	3.88E-05	286	3 cg1935618	3.66E-05	316	cg26500816	3.52E-05	346	cg26963271	3.39E-05
257	5 cg0128328	3.86E-05	287	9 cg0354432	3.66E-05	317	cg25538571	3.52E-05	347	cg01407797	3.39E-05
258	9 cg1054997	3.86E-05	288	0 cg0236464	3.66E-05	318	cg09915099	3.51E-05	348	cg08822227	3.38E-05
259	3 cg2525672	3.83E-05	289	2 cg1875578	3.64E-05	319	cg23428445	3.50E-05	349	cg06320982	3.38E-05
260	3 cg0392979	3.82E-05	290	3 cg0303075	3.64E-05	320	cg16614500	3.48E-05	350	cg05535113	3.38E-05
261	6 cg1385487	3.81E-05	291	7 cg0946257	3.63E-05	321	cg19235307	3.47E-05	351	cg21096915	3.36E-05
262	4 cg1433207	3.80E-05	292	6 cg0537935	3.63E-05	322	cg08876932	3.46E-05	352	cg03909500	3.36E-05
263	9 cg0194640	3.78E-05	293	0 cg0515861	3.63E-05	323	cg10235817	3.46E-05	353	cg06147863	3.36E-05
264	1 cg0129469	3.78E-05	294	5 cg2486053	3.60E-05	324	cg01459453	3.46E-05	354	cg20240860	3.36E-05
265	5 cg0712306	3.78E-05	295	4 cg1668290	3.60E-05	325	cg19055231	3.46E-05	355	cg03943081	3.35E-05
266	9 cg1857338	3.77E-05	296	3 cg0248955	3.60E-05	326	cg24851490	3.45E-05	356	cg01154193	3.35E-05
267	3 cg0140040	3.77E-05	297	2 cg2252734	3.60E-05	327	cg15839448	3.45E-05	357	cg06361108	3.34E-05
268	1 cg0004705	3.77E-05	298	5 cg2000833	3.59E-05	328	cg00489401	3.45E-05	358	cg24012925	3.33E-05
269	0 cg2350684	3.76E-05	299	2 cg0544290	3.59E-05	329	cg04062391	3.45E-05	359	cg17791651	3.33E-05
270	2 CpG site cg1236566	3.75E-05	300	2 cg1720759	3.59E-05	330	cg22396353	3.45E-05	360	cg20979799	3.32E-05
Ran k	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	
361	7 cg1703172	3.32E-05	391	0 cg0907212	3.22E-05	421	cg27389185	3.13E-05	451	cg26297688	3.07E-05
362	7 cg1805993	3.32E-05	392	0 cg1092753	3.21E-05	422	cg00308665	3.13E-05	452	cg25736482	3.06E-05
363	3 cg2594794	3.32E-05	393	6 cg2026473	3.21E-05	423	cg10150813	3.13E-05	453	cg00911351	3.06E-05
364	5 cg2576604	3.31E-05	394	2 cg2528241	3.20E-05	424	cg06433658	3.13E-05	454	cg05010623	3.05E-05
365	6 cg0942731	3.31E-05	395	0 cg1485941	3.20E-05	425	cg12758687	3.13E-05	455	cg11808757	3.05E-05
366	1 cg2630423	3.31E-05	396	7 cg1277484	3.20E-05	426	cg09262269	3.12E-05	456	cg05570980	3.05E-05
367	7 cg2274709	3.31E-05	397	5 cg1274142	3.20E-05	427	cg13885201	3.12E-05	457	cg00426498	3.04E-05
368	2 cg1971319	3.30E-05	398	0 cg0442462	3.20E-05	428	cg18787975	3.12E-05	458	cg05890019	3.04E-05
369	6 cg1940288	3.30E-05	399	1 cg1787897	3.19E-05	429	cg20973210	3.12E-05	459	cg14967066	3.04E-05
370	5 cg1931043	3.30E-05	400	2 cg2153089	3.19E-05	430	cg06971096	3.11E-05	460	cg18074297	3.04E-05
371	0 cg2465318	3.29E-05	401	0 cg2516689	3.19E-05	431	cg15563382	3.11E-05	461	cg19395441	3.04E-05
372	1 cg1994584	3.29E-05	402	6 cg1654302	3.19E-05	432	cg10281002	3.11E-05	462	cg03565323	3.03E-05
373	0 cg2187066	3.29E-05	403	7 cg2105704	3.18E-05	433	cg15982419	3.11E-05	463	cg17453778	3.03E-05
374	2 cg1590342	3.28E-05	404	6 cg0981647	3.18E-05	434	cg15928398	3.10E-05	464	cg24231716	3.03E-05
375	1 cg05473871	3.28E-05	405	1 cg17992056	3.18E-05	435	cg17992056	3.10E-05	465	cg05473871	3.03E-05

SUPPLEMENTARY DATA

	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e
376	cg0428938			cg1019381			cg11981599			cg22187630	
	5	3.28E-05	406	7	3.18E-05	436		3.10E-05	466		3.02E-05
377	cg1287070			cg2580209						cg05250458	
	5	3.28E-05	407	3	3.17E-05	437	cg00168942	3.09E-05	467		3.02E-05
378	cg0432945			cg0151974						cg07935568	
	4	3.27E-05	408	2	3.16E-05	438	cg25375711	3.09E-05	468		3.02E-05
379	cg2015824			cg1294136						cg02620013	
	8	3.26E-05	409	9	3.16E-05	439	cg12532500	3.09E-05	469		3.02E-05
380	cg1031950			cg2551142						cg21016177	
	5	3.26E-05	410	9	3.16E-05	440	cg10044101	3.09E-05	470		3.02E-05
381	cg1207892			cg0966017						cg03848555	
	9	3.25E-05	411	1	3.15E-05	441	cg00201234	3.08E-05	471		3.01E-05
382	cg1537751			cg2270522						cg18016365	
	8	3.25E-05	412	5	3.15E-05	442	cg07139440	3.08E-05	472		3.01E-05
383	cg0709940			cg1541550						cg21908259	
	7	3.24E-05	413	7	3.15E-05	443	cg22909609	3.08E-05	473		3.01E-05
384	cg0857052			cg0364122						cg24739326	
	1	3.24E-05	414	5	3.15E-05	444	cg20449692	3.08E-05	474		3.01E-05
385	cg1226178			cg1438669						cg18303397	
	6	3.24E-05	415	1	3.15E-05	445	cg15473868	3.08E-05	475		3.01E-05
386	cg0278948			cg0889694						cg10756887	
	5	3.23E-05	416	5	3.14E-05	446	cg02197293	3.07E-05	476		3.00E-05
387	cg1975906			cg2598338						cg17838026	
	4	3.23E-05	417	0	3.14E-05	447	cg22449114	3.07E-05	477		3.00E-05
388	cg2438467			cg2211580						cg13666340	
	6	3.23E-05	418	8	3.14E-05	448	cg05228408	3.07E-05	478		3.00E-05
389	cg0256452			cg1867818						cg10722799	
	3	3.22E-05	419	5	3.13E-05	449	cg16924616	3.07E-05	479		3.00E-05
390	cg0681064			cg1143842						cg01200177	
	7	3.22E-05	420	8	3.13E-05	450	cg12259537	3.07E-05	480		3.00E-05
Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e
	cg0385214			cg1503700							
481	4	2.99E-05	511	4	2.94E-05	541	cg13500819	2.88E-05	571	cg16776350	2.82E-05
	cg1851100			cg2383389							
482	7	2.99E-05	512	6	2.94E-05	542	cg06824727	2.88E-05	572	cg23265096	2.82E-05
	cg0020270			cg1086511							
483	2	2.99E-05	513	9	2.94E-05	543	cg00563926	2.88E-05	573	cg00548268	2.81E-05
	cg2682409			cg1486586							
484	1	2.99E-05	514	8	2.94E-05	544	cg08655844	2.88E-05	574	cg12052765	2.81E-05
	cg0284877			cg1028147							
485	7	2.99E-05	515	8	2.93E-05	545	cg07903918	2.88E-05	575	cg25302419	2.81E-05
	cg2505431			cg2594245							
486	1	2.98E-05	516	0	2.93E-05	546	cg04460372	2.87E-05	576	cg18765542	2.81E-05
	cg0802250			cg2261301							
487	2	2.98E-05	517	0	2.93E-05	547	cg16483916	2.87E-05	577	cg21289015	2.81E-05
	cg0208550			cg2290184							
488	7	2.98E-05	518	0	2.93E-05	548	cg11279021	2.87E-05	578	cg20043466	2.80E-05
	cg1068205			cg2000182							
489	7	2.98E-05	519	9	2.93E-05	549	cg11189837	2.87E-05	579	cg02071305	2.80E-05
	cg1008499			cg2560488							
490	3	2.98E-05	520	3	2.93E-05	550	cg27601516	2.87E-05	580	cg01805282	2.80E-05
	cg2099480			cg1251348							
491	1	2.98E-05	521	1	2.92E-05	551	cg24056567	2.86E-05	581	cg07442479	2.80E-05
	cg1515683			cg1389910							
492	6	2.98E-05	522	8	2.92E-05	552	cg20279283	2.86E-05	582	cg17431739	2.80E-05
	cg0626975			cg0587113							
493	3	2.98E-05	523	6	2.92E-05	553	cg16063112	2.86E-05	583	cg24642523	2.80E-05
	cg2268020			cg0548350							
494	4	2.98E-05	524	9	2.92E-05	554	cg24986868	2.86E-05	584	cg10240853	2.80E-05
	cg2603644			cg1625430							
495	3	2.97E-05	525	9	2.91E-05	555	cg00431114	2.86E-05	585	cg09595479	2.79E-05
	cg0282810			cg2728109							
496	4	2.97E-05	526	3	2.91E-05	556	cg00563932	2.86E-05	586	cg23320649	2.79E-05
	cg1627089			cg1255613							
497	0	2.97E-05	527	4	2.91E-05	557	cg19706682	2.85E-05	587	cg08996521	2.79E-05
	cg1732412			cg2090052							
498	8	2.97E-05	528	4	2.91E-05	558	cg15747595	2.85E-05	588	cg15776355	2.79E-05
	cg0830314			cg1158469							
499	6	2.97E-05	529	0	2.91E-05	559	cg16352283	2.85E-05	589	cg20654468	2.79E-05
	cg0719557			cg0360068							
500	7	2.97E-05	530	7	2.91E-05	560	cg26131019	2.85E-05	590	cg09429111	2.79E-05
	cg2571318			cg1928319							
501	5	2.97E-05	531	6	2.91E-05	561	cg06638433	2.84E-05	591	cg23850212	2.79E-05

SUPPLEMENTARY DATA

502	cg1482645 6 cg2716902 0	2.96E-05	532	cg0388351 9 cg1959466 6	2.90E-05	562	cg00689340	2.84E-05	592	cg16240480	2.79E-05
503	cg0743060 5	2.95E-05	533	cg1051595 6	2.90E-05	563	cg27187881	2.84E-05	593	cg07185695	2.78E-05
504	cg0949288 7	2.95E-05	534	cg1636213 3	2.90E-05	564	cg11879514	2.83E-05	594	cg12073594	2.78E-05
505	cg0501005 8	2.95E-05	535	cg0773778 1	2.90E-05	565	cg13593287	2.83E-05	595	cg15201635	2.78E-05
506	cg1022674 9	2.95E-05	536	cg1131468 4	2.89E-05	566	cg06948294	2.83E-05	596	cg23762517	2.78E-05
507	cg0220625 9	2.95E-05	537	cg1437779 1	2.89E-05	567	cg03565081	2.83E-05	597	cg15352829	2.78E-05
508	cg1747192 8	2.95E-05	538	cg1935519 0	2.89E-05	568	cg06161930	2.82E-05	598	cg20346726	2.78E-05
509	cg2063730 7	2.94E-05	539	cg1174749 9	2.89E-05	569	cg11010122	2.82E-05	599	cg11738543	2.77E-05
510	Ran k	Importanc e	Ran k	CpG site cg0378245 3	2.88E-05	570	cg24512400	2.82E-05	600	cg00208967	2.77E-05
601	CpG site cg1971346 0	2.77E-05	631	CpG site cg0165458 2	2.71E-05	661	cg09325711	2.64E-05	691	cg09563216	2.60E-05
602	cg0560071 7	2.77E-05	632	cg0382697 6	2.71E-05	662	cg23239396	2.64E-05	692	cg06144905	2.59E-05
603	cg0478685 7	2.77E-05	633	cg1487027 1	2.70E-05	663	cg14155397	2.64E-05	693	cg09706243	2.59E-05
604	cg0233544 1	2.76E-05	634	cg0265429 1	2.70E-05	664	cg17029151	2.64E-05	694	cg01919208	2.59E-05
605	cg1612784 5	2.76E-05	635	cg0403689 8	2.70E-05	665	cg13620770	2.64E-05	695	cg11428724	2.59E-05
606	cg2263193 8	2.76E-05	636	cg1499225 3	2.70E-05	666	cg15974053	2.64E-05	696	cg12928668	2.59E-05
607	cg2142638 7	2.76E-05	637	cg1261338 3	2.69E-05	667	cg01161216	2.64E-05	697	cg00090147	2.59E-05
608	cg2247229 0	2.76E-05	638	cg1091760 2	2.69E-05	668	cg08849574	2.64E-05	698	cg00630583	2.59E-05
609	cg0934063 9	2.76E-05	639	cg0765221 3	2.69E-05	669	cg00152644	2.63E-05	699	cg14958635	2.59E-05
610	cg0858786 4	2.76E-05	640	cg2182067 7	2.68E-05	670	cg17966619	2.63E-05	700	cg26083396	2.59E-05
611	cg1916833 8	2.76E-05	641	cg1468105 5	2.68E-05	671	cg26780333	2.63E-05	701	cg20080624	2.58E-05
612	cg2572584 3	2.76E-05	642	cg1963571 2	2.68E-05	672	cg20419410	2.63E-05	702	cg08370996	2.58E-05
613	cg2061641 4	2.75E-05	643	cg1372619 1	2.68E-05	673	cg20227766	2.63E-05	703	cg23430664	2.58E-05
614	cg0667547 8	2.75E-05	644	cg0516463 4	2.68E-05	674	cg24127989	2.63E-05	704	cg19889780	2.58E-05
615	cg2020900 9	2.75E-05	645	cg1915559 9	2.67E-05	675	cg23752923	2.63E-05	705	cg24200059	2.58E-05
616	cg0459812 1	2.75E-05	646	cg0126979 5	2.67E-05	676	cg15456206	2.63E-05	706	cg14100184	2.58E-05
617	cg0056416 3	2.75E-05	647	cg1976455 5	2.67E-05	677	cg24727203	2.62E-05	707	cg13047892	2.58E-05
618	cg2049664 3	2.75E-05	648	cg2223662 6	2.67E-05	678	cg04739570	2.62E-05	708	cg04457979	2.58E-05
619	cg0102773 9	2.75E-05	649	cg1126084 8	2.67E-05	679	cg05056120	2.61E-05	709	cg14056644	2.57E-05
620	cg0250385 0	2.74E-05	650	cg0762104 6	2.66E-05	680	cg17692403	2.61E-05	710	cg19669036	2.57E-05
621	cg1290203 9	2.74E-05	651	cg2271962 3	2.66E-05	681	cg17914753	2.60E-05	711	cg04597449	2.57E-05
622	cg0623849 1	2.74E-05	652	cg0908362 7	2.66E-05	682	cg27493997	2.60E-05	712	cg07979752	2.56E-05
623	cg2458726 8	2.73E-05	653	cg1183386 1	2.66E-05	683	cg02988947	2.60E-05	713	cg00685836	2.56E-05
624	cg0488006 3	2.73E-05	654	cg0158004 4	2.65E-05	684	cg02016419	2.60E-05	714	cg09079275	2.56E-05
625	cg2671182 0	2.72E-05	655	cg0554604 4	2.65E-05	685	cg10362591	2.60E-05	715	cg04726200	2.56E-05
626	cg2565509 6	2.72E-05	656	cg1374534 6	2.65E-05	686	cg22521310	2.60E-05	716	cg26673195	2.56E-05
627		2.72E-05	657		2.64E-05	687	cg06051311	2.60E-05	717	cg12069309	2.56E-05

SUPPLEMENTARY DATA

	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e
Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e
628	cg0960162 9	2.72E-05	658	cg2083170 8	2.64E-05	688	cg02515725	2.60E-05	718	cg23283875	2.56E-05
629	cg1923392 3	2.72E-05	659	cg0855565 7	2.64E-05	689	cg22321558	2.60E-05	719	cg02994956	2.55E-05
630	cg2562969 4	2.72E-05	660	cg1957316 6	2.64E-05	690	cg07588779	2.60E-05	720	cg21480743	2.55E-05
Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e
	cg1189627 1	2.55E-05	751	cg2297119 1	2.52E-05	781	cg02776251	2.48E-05	811	cg16761581	2.45E-05
721	cg0218150 6	2.55E-05	752	cg2243622 9	2.52E-05	782	cg10104451	2.48E-05	812	cg07314414	2.45E-05
722	cg0049725 1	2.55E-05	753	cg0160018 9	2.52E-05	783	cg15945417	2.48E-05	813	cg03945800	2.45E-05
723	cg2180805 3	2.55E-05	754	cg0065121 6	2.51E-05	784	cg17589341	2.48E-05	814	cg26512148	2.44E-05
724	cg1531633 4	2.55E-05	755	cg2407688 4	2.51E-05	785	cg06253072	2.47E-05	815	cg23047271	2.44E-05
725	cg1640897 0	2.55E-05	756	cg1295558 3	2.51E-05	786	cg24173049	2.47E-05	816	cg02774439	2.44E-05
726	cg1526166 5	2.54E-05	757	cg0376048 3	2.51E-05	787	cg02062650	2.47E-05	817	cg06621358	2.43E-05
727	cg0537345 7	2.54E-05	758	cg0639224 1	2.51E-05	788	cg03138091	2.47E-05	818	cg05898524	2.43E-05
728	cg2548300 3	2.54E-05	759	cg2442983 5	2.51E-05	789	cg07973967	2.47E-05	819	cg01346152	2.43E-05
729	cg0111408 8	2.54E-05	760	cg2375848 6	2.51E-05	790	cg15853125	2.47E-05	820	cg20557202	2.43E-05
730	cg1903716 7	2.54E-05	761	cg0784616 5	2.50E-05	791	cg06236061	2.47E-05	821	cg17943999	2.43E-05
731	cg0225560 9	2.54E-05	762	cg2210114 7	2.50E-05	792	cg18555440	2.47E-05	822	cg00398048	2.43E-05
732	cg1164828 9	2.54E-05	763	cg1972822 7	2.50E-05	793	cg00282347	2.46E-05	823	cg08441806	2.43E-05
733	cg0958204 2	2.54E-05	764	cg0746979 3	2.50E-05	794	cg11223252	2.46E-05	824	cg12600197	2.43E-05
734	cg2135323 2	2.54E-05	765	cg01017147 2	2.50E-05	795	cg01017147	2.46E-05	825	cg00187380	2.43E-05
735	cg2601890 1	2.53E-05	766	cg1331144 0	2.49E-05	796	cg06117855	2.46E-05	826	cg16998353	2.43E-05
736	cg2181825 7	2.53E-05	767	cg0748293 6	2.49E-05	797	cg24768561	2.46E-05	827	cg26509022	2.43E-05
737	cg1434853 2	2.53E-05	768	cg2464641 4	2.49E-05	798	cg02276665	2.46E-05	828	cg04466273	2.43E-05
738	cg1356515 7	2.53E-05	769	cg2692868 2	2.49E-05	799	cg21509097	2.46E-05	829	cg14093936	2.43E-05
739	cg0276461 1	2.53E-05	770	cg1638608 0	2.49E-05	800	cg18972811	2.46E-05	830	cg00472814	2.43E-05
740	cg0548863 2	2.53E-05	771	cg0354779 7	2.49E-05	801	cg00576250	2.46E-05	831	cg27236973	2.43E-05
741	cg2112024 9	2.53E-05	772	cg0663024 1	2.49E-05	802	cg09155852	2.46E-05	832	cg23786576	2.42E-05
742	cg0856967 8	2.53E-05	773	cg0809788 2	2.48E-05	803	cg02254649	2.46E-05	833	cg12457773	2.42E-05
743	cg2662413 4	2.53E-05	774	cg0864698 8	2.48E-05	804	cg07495664	2.46E-05	834	cg09863772	2.42E-05
744	cg1316372 9	2.52E-05	775	cg1783030 8	2.48E-05	805	cg24450312	2.46E-05	835	cg26209676	2.42E-05
745	cg0775364 4	2.52E-05	776	cg2002847 0	2.48E-05	806	cg15271616	2.46E-05	836	cg10194829	2.42E-05
746	cg0615457 0	2.52E-05	777	cg1572053 5	2.48E-05	807	cg26968812	2.45E-05	837	cg21073927	2.42E-05
747	cg0529424 3	2.52E-05	778	cg2160404 2	2.48E-05	808	cg05786809	2.45E-05	838	cg27626102	2.42E-05
748	cg2258051 2	2.52E-05	779	cg2480121 0	2.48E-05	809	cg11469321	2.45E-05	839	cg21402071	2.42E-05
749	cg0010718 7	2.52E-05	780	cg1497399 5	2.48E-05	810	cg07558455	2.45E-05	840	cg17165284	2.42E-05
Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e	Ran k	CpG site	Importanc e
	cg1633257 7	2.41E-05	871	cg2374873 7	2.39E-05	901	cg01655355	2.36E-05	931	cg04409945	2.33E-05
841	cg1454029 7	2.41E-05	872	cg1946401 6	2.39E-05	902	cg03775422	2.36E-05	932	cg08654655	2.32E-05

SUPPLEMENTARY DATA

	CpG site	Importance		CpG site	Importance		CpG site	Importance		CpG site	Importance
Rank	CpG site	Importance	Rank	CpG site	Importance	Rank	CpG site	Importance	Rank	CpG site	Importance
843	cg1742162 3	2.41E-05	873	cg2300290 7	2.39E-05	903	cg01441777	2.36E-05	933	cg21176048	2.32E-05
844	cg2197476 6	2.41E-05	874	cg1642767 0	2.39E-05	904	cg20723355	2.36E-05	934	cg12331389	2.32E-05
845	cg0219665 5	2.41E-05	875	cg0638508 7	2.39E-05	905	cg01791232	2.36E-05	935	cg27631256	2.32E-05
846	cg2620234 0	2.41E-05	876	cg1064890 8	2.38E-05	906	cg22215728	2.36E-05	936	cg18081258	2.32E-05
847	cg2637410 1	2.41E-05	877	cg1846413 7	2.38E-05	907	cg24207176	2.36E-05	937	cg07991621	2.32E-05
848	cg1148087 3	2.41E-05	878	cg0628835 1	2.38E-05	908	cg13262687	2.36E-05	938	cg22799850	2.32E-05
849	cg0734909 4	2.41E-05	879	cg0411431 5	2.38E-05	909	cg12564453	2.36E-05	939	cg08097755	2.32E-05
850	cg1536461 8	2.41E-05	880	cg0403222 6	2.38E-05	910	cg11296937	2.36E-05	940	cg24874111	2.31E-05
851	cg2505002 6	2.41E-05	881	cg2314635 8	2.38E-05	911	cg14972143	2.35E-05	941	cg08587542	2.31E-05
852	cg0572406 5	2.40E-05	882	cg1110889 0	2.38E-05	912	cg11041457	2.35E-05	942	cg25713309	2.31E-05
853	cg1017579 5	2.40E-05	883	cg1115872 9	2.38E-05	913	cg24107665	2.35E-05	943	cg01353448	2.31E-05
854	cg1733840 3	2.40E-05	884	cg1008000 4	2.38E-05	914	cg00653387	2.35E-05	944	cg20506783	2.31E-05
855	cg0500114 5	2.40E-05	885	cg1005284 0	2.38E-05	915	cg05073035	2.35E-05	945	cg04588079	2.31E-05
856	cg1716999 8	2.40E-05	886	cg0039948 3	2.38E-05	916	cg16404106	2.35E-05	946	cg26898166	2.31E-05
857	cg1323486 3	2.40E-05	887	cg0576916 1	2.38E-05	917	cg16954341	2.35E-05	947	cg05157725	2.31E-05
858	cg0586879 9	2.40E-05	888	cg0857261 1	2.38E-05	918	cg21926138	2.35E-05	948	cg08197122	2.31E-05
859	cg2194978 1	2.40E-05	889	cg2627074 6	2.37E-05	919	cg02755525	2.34E-05	949	cg00565075	2.31E-05
860	cg1725296 0	2.40E-05	890	cg0691108 4	2.37E-05	920	cg26093148	2.34E-05	950	cg10331779	2.30E-05
861	cg1354836 1	2.40E-05	891	cg1867876 3	2.37E-05	921	cg03889226	2.34E-05	951	cg02782630	2.30E-05
862	cg1500343 4	2.40E-05	892	cg1098951 7	2.37E-05	922	cg16984944	2.34E-05	952	cg20083676	2.30E-05
863	cg1028713 7	2.40E-05	893	cg1672184 5	2.37E-05	923	cg14913610	2.34E-05	953	cg12478185	2.30E-05
864	cg0872451 7	2.40E-05	894	cg0784539 2	2.37E-05	924	cg10893437	2.34E-05	954	cg05824484	2.30E-05
865	cg2737627 1	2.40E-05	895	cg1343883 4	2.37E-05	925	cg13526007	2.34E-05	955	cg24641352	2.30E-05
866	cg0337913 1	2.40E-05	896	cg1628429 2	2.36E-05	926	cg16718678	2.33E-05	956	cg08162780	2.30E-05
867	cg2626143 1	2.39E-05	897	cg0488727 8	2.36E-05	927	cg19596204	2.33E-05	957	cg02260587	2.30E-05
868	cg2154770 8	2.39E-05	898	cg1390449 3	2.36E-05	928	cg06885782	2.33E-05	958	cg24649713	2.30E-05
869	cg1136864 3	2.39E-05	899	cg0592458 3	2.36E-05	929	cg05507459	2.33E-05	959	cg20051033	2.30E-05
870	cg1647469 6	2.39E-05	900	cg2412564 8	2.36E-05	930	cg19192120	2.33E-05	960	cg05697231	2.30E-05
Rank	CpG site	Importance	Rank	CpG site	Importance	Rank	CpG site	Importance	Rank	CpG site	Importance
961	cg21092687	2.30E-05	991	cg13818573	2.26E-05						
962	cg14244577	2.30E-05	992	cg26581729	2.26E-05						
963	cg14329157	2.30E-05	993	cg10521852	2.26E-05						
964	cg18809289	2.29E-05	994	cg11386746	2.26E-05						
965	cg13150977	2.29E-05	995	cg13806135	2.26E-05						
966	cg10986043	2.29E-05	996	cg21053529	2.26E-05						
967	cg21152671	2.29E-05	997	cg00650762	2.25E-05						
968	cg26984624	2.29E-05	998	cg22183706	2.25E-05						
969	cg24101578	2.29E-05	999	cg20537629	2.25E-05						
970	cg20716064	2.29E-05	1000	cg08331960	2.25E-05						

SUPPLEMENTARY DATA

971	cg02994974	2.29E-05
972	cg17655614	2.29E-05
973	cg22799321	2.28E-05
974	cg16413777	2.28E-05
975	cg17775235	2.28E-05
976	cg21972382	2.28E-05
977	cg10064162	2.28E-05
978	cg08858521	2.28E-05
979	cg24596472	2.28E-05
980	cg16774604	2.28E-05
981	cg10106284	2.28E-05
982	cg18993334	2.27E-05
983	cg16519321	2.27E-05
984	cg00582628	2.27E-05
985	cg05194726	2.27E-05
986	cg24715735	2.27E-05
987	cg04587910	2.27E-05
988	cg17241310	2.27E-05
989	cg14380517	2.27E-05
990	cg23771661	2.27E-05

Supplementary Table 3. Gene enrichment report obtained with Gene Ontology.

GO biological process complete	Homo sapiens - REFLIST (20851)	# (out of 849 uploaded)	# (expected)	over/under	Fold Enrichment	raw P-value	FDR
system development (GO:0048731)	4460	302	181.6	+	1.66	2.52E-20	4.02E-16
neurogenesis (GO:0022008)	1669	152	67.96	+	2.24	1.41E-19	1.12E-15
multicellular organism development (GO:0007275)	5080	328	206.84	+	1.59	2.51E-19	1.33E-15
generation of neurons (GO:0048699)	1565	145	63.72	+	2.28	2.60E-19	1.04E-15
anatomical structure development (GO:0048856)	5469	346	222.68	+	1.55	2.85E-19	9.09E-16
nervous system development (GO:0007399)	2395	191	97.52	+	1.96	9.46E-19	2.52E-15
regulation of multicellular organismal process (GO:0051239)	3211	233	130.74	+	1.78	2.50E-18	5.70E-15
developmental process (GO:0032502)	5918	363	240.97	+	1.51	2.83E-18	5.64E-15
biological regulation (GO:0065007)	12525	633	509.99	+	1.24	3.51E-18	6.22E-15

SUPPLEMENTARY DATA

neuron differentiation (GO:0030182)	1021	107	41.57	+	2.57	1.10E-17	1.76E-14
multicellular organismal process (GO:0032501)	7037	410	286.53	+	1.43	1.33E-17	1.94E-14
cellular process (GO:0009987)	15458	732	629.41	+	1.16	4.76E-17	6.33E-14
Unclassified (UNCLASSIFIED)	3041	46	123.82	-	0.37	8.99E-17	1.10E-13
biological_process (GO:0008150)	17810	803	725.18	+	1.11	8.99E-17	1.02E-13
animal organ development (GO:0048513)	3225	227	131.31	+	1.73	2.04E-16	2.17E-13
cell differentiation (GO:0030154)	3744	251	152.45	+	1.65	7.31E-16	7.30E-13
anatomical structure morphogenesis (GO:0009653)	2181	170	88.8	+	1.91	1.23E-15	1.16E-12
cellular developmental process (GO:0048869)	3798	252	154.64	+	1.63	2.17E-15	1.92E-12
regulation of localization (GO:0032879)	2838	202	115.56	+	1.75	6.47E-15	5.44E-12
regulation of biological process (GO:0050789)	11825	592	481.48	+	1.23	2.70E-14	2.15E-11
regulation of biological quality (GO:0065008)	4134	264	168.33	+	1.57	3.14E-14	2.38E-11
regulation of developmental process (GO:0050793)	2651	188	107.94	+	1.74	1.39E-13	1.01E-10
regulation of cellular process (GO:0050794)	11288	567	459.62	+	1.23	2.60E-13	1.80E-10
animal organ morphogenesis (GO:0009887)	973	93	39.62	+	2.35	2.99E-13	1.99E-10
signaling (GO:0023052)	5504	323	224.11	+	1.44	4.78E-13	3.05E-10
regulation of multicellular organismal development (GO:2000026)	2082	155	84.77	+	1.83	1.18E-12	7.23E-10
cell communication (GO:0007154)	5610	324	228.43	+	1.42	2.83E-12	1.67E-09
cellular response to stimulus (GO:0051716)	6801	374	276.92	+	1.35	1.05E-11	5.99E-09
regulation of cell differentiation (GO:0045595)	1857	139	75.61	+	1.84	1.55E-11	8.52E-09
response to stimulus (GO:0050896)	8572	449	349.03	+	1.29	1.57E-11	8.35E-09
regulation of cell development (GO:0060284)	966	88	39.33	+	2.24	1.62E-11	8.37E-09
cellular response to organic substance (GO:0071310)	2400	167	97.72	+	1.71	1.79E-11	8.94E-09
response to endogenous stimulus (GO:0009719)	1512	119	61.56	+	1.93	2.74E-11	1.32E-08
behavior (GO:0007610)	600	64	24.43	+	2.62	3.18E-11	1.49E-08
regulation of neurogenesis (GO:0050767)	840	79	34.2	+	2.31	4.67E-11	2.13E-08
positive regulation of multicellular organismal process (GO:0051240)	1783	133	72.6	+	1.83	5.58E-11	2.48E-08
neuron development (GO:0048666)	828	78	33.71	+	2.31	6.03E-11	2.60E-08
negative regulation of multicellular organismal process (GO:0051241)	1224	102	49.84	+	2.05	6.18E-11	2.59E-08
regulation of cell communication (GO:0010646)	3646	227	148.46	+	1.53	6.44E-11	2.63E-08

SUPPLEMENTARY DATA

regulation of signaling (GO:0023051)	3686	228	150.08	+	1.52	1.05E-10	4.20E-08
regulation of nervous system development (GO:0051960)	952	85	38.76	+	2.19	1.10E-10	4.27E-08
positive regulation of biological process (GO:0048518)	6278	346	255.62	+	1.35	1.14E-10	4.31E-08
signal transduction (GO:0007165)	5146	295	209.53	+	1.41	1.46E-10	5.40E-08
positive regulation of cellular process (GO:0048522)	5725	321	233.11	+	1.38	1.63E-10	5.90E-08
cell development (GO:0048468)	1632	123	66.45	+	1.85	1.91E-10	6.78E-08
central nervous system development (GO:0007417)	1001	87	40.76	+	2.13	1.97E-10	6.82E-08
positive regulation of developmental process (GO:0051094)	1401	110	57.05	+	1.93	2.23E-10	7.57E-08
regulation of transport (GO:0051049)	1906	137	77.61	+	1.77	3.01E-10	1.00E-07
neuron projection development (GO:0031175)	683	67	27.81	+	2.41	3.03E-10	9.88E-08
response to organic substance (GO:0010033)	3033	194	123.5	+	1.57	3.19E-10	1.02E-07
cellular response to endogenous stimulus (GO:0071495)	1224	99	49.84	+	1.99	4.47E-10	1.40E-07
localization (GO:0051179)	5802	321	236.24	+	1.36	6.92E-10	2.12E-07
cellular response to chemical stimulus (GO:0070887)	2961	189	120.56	+	1.57	7.59E-10	2.29E-07
negative regulation of biological process (GO:0048519)	5541	308	225.62	+	1.37	1.36E-09	4.03E-07
regulation of cell population proliferation (GO:0042127)	1656	121	67.43	+	1.79	1.39E-09	4.03E-07
negative regulation of developmental process (GO:0051093)	972	83	39.58	+	2.1	1.44E-09	4.11E-07
locomotion (GO:0040011)	1314	102	53.5	+	1.91	1.73E-09	4.85E-07
positive regulation of cell differentiation (GO:0045597)	1001	83	40.76	+	2.04	4.35E-09	1.20E-06
regulation of response to stimulus (GO:0048583)	4403	254	179.28	+	1.42	4.41E-09	1.19E-06
tissue development (GO:0009888)	1789	126	72.84	+	1.73	5.00E-09	1.33E-06
detection of chemical stimulus involved in sensory perception (GO:0050907)	483	0	19.67	-	< 0.01	6.92E-09	1.81E-06
cell fate commitment (GO:0045165)	252	34	10.26	+	3.31	8.81E-09	2.27E-06
embryonic organ development (GO:0048568)	447	48	18.2	+	2.64	9.85E-09	2.49E-06
cell migration (GO:0016477)	957	79	38.97	+	2.03	1.42E-08	3.53E-06
negative regulation of neurogenesis (GO:0050768)	292	36	11.89	+	3.03	2.66E-08	6.53E-06
neuron projection morphogenesis (GO:0048812)	494	50	20.11	+	2.49	2.84E-08	6.87E-06

SUPPLEMENTARY DATA

negative regulation of cell development (GO:0010721)	335	39	13.64	+	2.86	2.88E-08	6.85E-06
detection of chemical stimulus involved in sensory perception of smell (GO:0050911)	439	0	17.87	-	< 0.01	3.28E-08	7.71E-06
plasma membrane bounded cell projection morphogenesis (GO:0120039)	498	50	20.28	+	2.47	3.32E-08	7.68E-06
central nervous system neuron differentiation (GO:0021953)	190	28	7.74	+	3.62	3.42E-08	7.80E-06
cellular response to oxygen-containing compound (GO:1901701)	1080	85	43.97	+	1.93	3.58E-08	8.04E-06
cell projection morphogenesis (GO:0048858)	502	50	20.44	+	2.45	3.95E-08	8.76E-06
negative regulation of cell differentiation (GO:0045596)	715	63	29.11	+	2.16	4.74E-08	1.04E-05
regulation of signal transduction (GO:0009966)	3160	190	128.67	+	1.48	5.07E-08	1.09E-05
negative regulation of cellular process (GO:0048523)	4888	270	199.03	+	1.36	5.21E-08	1.11E-05
negative regulation of nervous system development (GO:0051961)	315	37	12.83	+	2.88	5.30E-08	1.11E-05
regulation of cellular component movement (GO:0051270)	1027	81	41.82	+	1.94	6.58E-08	1.36E-05
cell part morphogenesis (GO:0032990)	524	51	21.34	+	2.39	7.44E-08	1.52E-05
tube development (GO:0035295)	859	71	34.98	+	2.03	8.40E-08	1.70E-05
response to organonitrogen compound (GO:0010243)	1014	80	41.29	+	1.94	8.65E-08	1.73E-05
embryo development (GO:0009790)	1016	80	41.37	+	1.93	8.86E-08	1.75E-05
regulation of neuron differentiation (GO:0045664)	672	60	27.36	+	2.19	8.97E-08	1.75E-05
embryonic morphogenesis (GO:0048598)	581	54	23.66	+	2.28	1.04E-07	2.01E-05
cell-cell signaling (GO:0007267)	1175	88	47.84	+	1.84	1.25E-07	2.37E-05
movement of cell or subcellular component (GO:0006928)	1570	109	63.93	+	1.71	1.31E-07	2.46E-05
cell morphogenesis involved in neuron differentiation (GO:0048667)	445	45	18.12	+	2.48	1.68E-07	3.13E-05
regulation of anatomical structure morphogenesis (GO:0022603)	1107	84	45.07	+	1.86	1.87E-07	3.44E-05
sensory organ development (GO:0007423)	560	52	22.8	+	2.28	1.99E-07	3.61E-05
embryonic organ morphogenesis (GO:0048562)	305	35	12.42	+	2.82	2.02E-07	3.62E-05
localization of cell (GO:0051674)	1078	82	43.89	+	1.87	2.04E-07	3.62E-05
cell motility (GO:0048870)	1078	82	43.89	+	1.87	2.04E-07	3.58E-05
positive regulation of cell development (GO:0010720)	564	52	22.96	+	2.26	2.25E-07	3.90E-05

SUPPLEMENTARY DATA

mesenchymal cell development (GO:0014031)	81	17	3.3	+	5.15	2.35E-07	4.03E-05
cellular response to drug (GO:0035690)	411	42	16.73	+	2.51	2.44E-07	4.14E-05
response to oxygen-containing compound (GO:1901700)	1609	110	65.51	+	1.68	2.51E-07	4.21E-05
response to drug (GO:0042493)	1030	79	41.94	+	1.88	2.62E-07	4.35E-05
sensory organ morphogenesis (GO:0090596)	268	32	10.91	+	2.93	3.01E-07	4.95E-05
regulation of ion transport (GO:0043269)	705	60	28.71	+	2.09	3.18E-07	5.18E-05
cell junction organization (GO:0034330)	490	47	19.95	+	2.36	3.49E-07	5.63E-05
response to organic cyclic compound (GO:0014070)	930	73	37.87	+	1.93	3.97E-07	6.33E-05
anatomical structure formation involved in morphogenesis (GO:0048646)	898	71	36.56	+	1.94	3.99E-07	6.31E-05
negative regulation of cellular component movement (GO:0051271)	315	35	12.83	+	2.73	4.04E-07	6.33E-05
cellular component morphogenesis (GO:0032989)	613	54	24.96	+	2.16	4.44E-07	6.87E-05
cell morphogenesis (GO:0000902)	729	61	29.68	+	2.06	4.75E-07	7.28E-05
neural crest cell differentiation (GO:0014033)	86	17	3.5	+	4.85	4.91E-07	7.47E-05
axon development (GO:0061564)	416	42	16.94	+	2.48	5.02E-07	7.56E-05
regulation of locomotion (GO:0040012)	982	75	39.98	+	1.88	5.54E-07	8.26E-05
response to growth factor (GO:0070848)	531	49	21.62	+	2.27	5.67E-07	8.38E-05
positive regulation of cell population proliferation (GO:0008284)	925	72	37.66	+	1.91	5.81E-07	8.50E-05
neural crest cell development (GO:0014032)	77	16	3.14	+	5.1	5.94E-07	8.62E-05
cellular component organization (GO:0016043)	5536	293	225.41	+	1.3	6.04E-07	8.68E-05
ossification (GO:0001503)	264	31	10.75	+	2.88	6.37E-07	9.08E-05
response to nitrogen compound (GO:1901698)	1098	81	44.71	+	1.81	8.74E-07	1.23E-04
pattern specification process (GO:0007389)	432	42	17.59	+	2.39	8.82E-07	1.23E-04
respiratory system development (GO:0060541)	200	26	8.14	+	3.19	9.22E-07	1.28E-04
stem cell development (GO:0048864)	81	16	3.3	+	4.85	1.07E-06	1.47E-04
response to chemical (GO:0042221)	4520	246	184.04	+	1.34	1.08E-06	1.47E-04
neural crest cell migration (GO:0001755)	52	13	2.12	+	6.14	1.15E-06	1.55E-04
circulatory system development (GO:0072359)	876	68	35.67	+	1.91	1.18E-06	1.59E-04
response to alcohol (GO:0097305)	245	29	9.98	+	2.91	1.26E-06	1.67E-04
forebrain development (GO:0030900)	404	40	16.45	+	2.43	1.26E-06	1.67E-04
positive regulation of neurogenesis (GO:0050769)	488	45	19.87	+	2.26	1.32E-06	1.72E-04
brain development (GO:0007420)	757	61	30.82	+	1.98	1.34E-06	1.74E-04

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chemical synaptic transmission (GO:0007268)	426	41	17.35	+	2.36	1.47E-06	1.89E-04
anterograde trans-synaptic signaling (GO:0098916)	426	41	17.35	+	2.36	1.47E-06	1.87E-04
cellular response to growth factor stimulus (GO:0071363)	502	46	20.44	+	2.25	1.61E-06	2.04E-04
negative regulation of response to stimulus (GO:0048585)	1836	118	74.76	+	1.58	1.66E-06	2.08E-04
synapse organization (GO:0050808)	293	32	11.93	+	2.68	1.76E-06	2.20E-04
modulation of chemical synaptic transmission (GO:0050804)	459	43	18.69	+	2.3	1.79E-06	2.22E-04
positive regulation of nervous system development (GO:0051962)	556	49	22.64	+	2.16	1.80E-06	2.21E-04
G protein-coupled receptor signaling pathway, coupled to cyclic nucleotide second messenger (GO:0007187)	250	29	10.18	+	2.85	1.82E-06	2.21E-04
regulation of cell motility (GO:2000145)	942	71	38.36	+	1.85	1.82E-06	2.20E-04
plasma membrane bounded cell projection organization (GO:0120036)	1126	81	45.85	+	1.77	1.84E-06	2.21E-04
regulation of trans-synaptic signaling (GO:0099177)	460	43	18.73	+	2.3	1.86E-06	2.21E-04
regionalization (GO:0003002)	336	35	13.68	+	2.56	1.90E-06	2.25E-04
muscle system process (GO:0003012)	295	32	12.01	+	2.66	2.01E-06	2.36E-04
negative regulation of cell population proliferation (GO:0008285)	698	57	28.42	+	2.01	2.12E-06	2.47E-04
positive regulation of cell communication (GO:0010647)	1943	123	79.11	+	1.55	2.17E-06	2.51E-04
regulation of system process (GO:0044057)	592	51	24.1	+	2.12	2.19E-06	2.52E-04
regulation of ossification (GO:0030278)	197	25	8.02	+	3.12	2.20E-06	2.51E-04
trans-synaptic signaling (GO:0099537)	445	42	18.12	+	2.32	2.23E-06	2.52E-04
negative regulation of developmental growth (GO:0048640)	109	18	4.44	+	4.06	2.28E-06	2.56E-04
axonogenesis (GO:0007409)	380	38	15.47	+	2.46	2.29E-06	2.56E-04
cell junction assembly (GO:0034329)	268	30	10.91	+	2.75	2.35E-06	2.60E-04
circulatory system process (GO:0003013)	402	39	16.37	+	2.38	2.38E-06	2.62E-04
regulation of hormone levels (GO:0010817)	546	48	22.23	+	2.16	2.50E-06	2.74E-04
chemotaxis (GO:0006935)	547	48	22.27	+	2.16	2.57E-06	2.79E-04
diencephalon development (GO:0021536)	77	15	3.14	+	4.78	2.68E-06	2.89E-04
cell projection organization (GO:0030030)	1171	83	47.68	+	1.74	2.69E-06	2.88E-04
taxis (GO:0042330)	549	48	22.35	+	2.15	2.71E-06	2.89E-04

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synaptic signaling (GO:0099536)	470	43	19.14	+	2.25	2.74E-06	2.89E-04
locomotory behavior (GO:0007626)	200	25	8.14	+	3.07	2.81E-06	2.95E-04
regulation of cell migration (GO:0030334)	879	67	35.79	+	1.87	2.82E-06	2.94E-04
cellular component organization or biogenesis (GO:0071840)	5754	298	234.29	+	1.27	3.22E-06	3.34E-04
cellular response to organonitrogen compound (GO:0071417)	606	51	24.67	+	2.07	3.23E-06	3.33E-04
blood circulation (GO:0008015)	392	38	15.96	+	2.38	3.33E-06	3.41E-04
negative regulation of locomotion (GO:0040013)	313	33	12.74	+	2.59	3.36E-06	3.41E-04
system process (GO:0003008)	1989	124	80.99	+	1.53	3.77E-06	3.80E-04
head development (GO:0060322)	802	62	32.66	+	1.9	4.01E-06	4.02E-04
positive regulation of signaling (GO:0023056)	1951	122	79.44	+	1.54	4.10E-06	4.09E-04
positive regulation of gene expression (GO:0010628)	2038	126	82.98	+	1.52	4.73E-06	4.69E-04
positive regulation of transcription, DNA-templated (GO:0045893)	1560	102	63.52	+	1.61	4.95E-06	4.88E-04
negative regulation of transport (GO:0051051)	500	44	20.36	+	2.16	5.43E-06	5.31E-04
detection of stimulus involved in sensory perception (GO:0050906)	546	4	22.23	-	0.18	5.79E-06	5.64E-04
regulation of molecular function (GO:0065009)	3073	175	125.12	+	1.4	6.02E-06	5.82E-04
cell morphogenesis involved in differentiation (GO:0000904)	565	48	23.01	+	2.09	6.21E-06	5.97E-04
positive regulation of signal transduction (GO:0009967)	1709	109	69.59	+	1.57	6.54E-06	6.25E-04
positive regulation of molecular function (GO:0044093)	1832	115	74.59	+	1.54	7.05E-06	6.70E-04
response to toxic substance (GO:0009636)	520	45	21.17	+	2.13	7.41E-06	7.00E-04
regulation of anatomical structure size (GO:0090066)	521	45	21.21	+	2.12	7.61E-06	7.14E-04
chemical homeostasis (GO:0048878)	1131	79	46.05	+	1.72	8.11E-06	7.57E-04
RNA processing (GO:0006396)	911	13	37.09	-	0.35	8.20E-06	7.61E-04
regulation of neurotransmitter levels (GO:0001505)	359	35	14.62	+	2.39	8.29E-06	7.65E-04
cellular response to nitrogen compound (GO:1901699)	663	53	27	+	1.96	8.41E-06	7.72E-04
ion homeostasis (GO:0050801)	798	61	32.49	+	1.88	8.41E-06	7.67E-04
lung development (GO:0030324)	173	22	7.04	+	3.12	8.56E-06	7.76E-04
growth (GO:0040007)	405	38	16.49	+	2.3	8.86E-06	7.99E-04
regulation of secretion (GO:0051046)	837	63	34.08	+	1.85	8.95E-06	8.02E-04

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ameboidal-type cell migration (GO:0001667)	174	22	7.08	+	3.11	9.29E-06	8.29E-04
regulation of cellular localization (GO:0060341)	1026	73	41.78	+	1.75	9.56E-06	8.48E-04
adult behavior (GO:0030534)	148	20	6.03	+	3.32	9.76E-06	8.61E-04
regulation of response to external stimulus (GO:0032101)	1196	82	48.7	+	1.68	9.89E-06	8.68E-04
ear development (GO:0043583)	231	26	9.41	+	2.76	9.97E-06	8.70E-04
camera-type eye morphogenesis (GO:0048593)	124	18	5.05	+	3.57	1.13E-05	9.80E-04
regulation of blood vessel diameter (GO:0097746)	137	19	5.58	+	3.41	1.16E-05	1.00E-03
regulation of tube diameter (GO:0035296)	137	19	5.58	+	3.41	1.16E-05	9.99E-04
mesenchyme development (GO:0060485)	219	25	8.92	+	2.8	1.18E-05	1.01E-03
respiratory tube development (GO:0030323)	177	22	7.21	+	3.05	1.18E-05	1.01E-03
homeostatic process (GO:0042592)	1668	106	67.92	+	1.56	1.24E-05	1.05E-03
cellular response to alcohol (GO:0097306)	89	15	3.62	+	4.14	1.26E-05	1.06E-03
regulation of tube size (GO:0035150)	138	19	5.62	+	3.38	1.28E-05	1.07E-03
neuromuscular process (GO:0050905)	113	17	4.6	+	3.69	1.30E-05	1.08E-03
synapse assembly (GO:0007416)	101	16	4.11	+	3.89	1.31E-05	1.08E-03
response to lipid (GO:0033993)	869	64	35.38	+	1.81	1.32E-05	1.08E-03
cellular response to organic cyclic compound (GO:0071407)	550	46	22.39	+	2.05	1.32E-05	1.08E-03
heart morphogenesis (GO:0003007)	250	27	10.18	+	2.65	1.34E-05	1.09E-03
negative regulation of growth (GO:0045926)	250	27	10.18	+	2.65	1.34E-05	1.08E-03
developmental growth (GO:0048589)	399	37	16.25	+	2.28	1.36E-05	1.10E-03
positive regulation of macromolecule metabolic process (GO:0010604)	3417	189	139.13	+	1.36	1.43E-05	1.15E-03
mesenchymal cell differentiation (GO:0048762)	153	20	6.23	+	3.21	1.51E-05	1.21E-03
response to hormone (GO:0009725)	924	67	37.62	+	1.78	1.56E-05	1.24E-03
detection of chemical stimulus (GO:0009593)	519	4	21.13	-	0.19	1.69E-05	1.33E-03
limb development (GO:0060173)	182	22	7.41	+	2.97	1.75E-05	1.38E-03
appendage development (GO:0048736)	182	22	7.41	+	2.97	1.75E-05	1.37E-03
sensory perception of smell (GO:0007608)	468	3	19.06	-	0.16	1.77E-05	1.38E-03
negative regulation of neuron differentiation (GO:0045665)	225	25	9.16	+	2.73	1.79E-05	1.39E-03
tube morphogenesis (GO:0035239)	659	52	26.83	+	1.94	1.80E-05	1.39E-03
positive regulation of nitrogen compound metabolic process (GO:0051173)	3239	180	131.88	+	1.36	1.81E-05	1.39E-03

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vascular process in circulatory system (GO:0003018)	169	21	6.88	+	3.05	1.86E-05	1.42E-03
negative regulation of cell communication (GO:0010648)	1428	93	58.14	+	1.6	1.88E-05	1.43E-03
negative regulation of signaling (GO:0023057)	1432	93	58.31	+	1.59	1.94E-05	1.46E-03
RNA metabolic process (GO:0016070)	1702	37	69.3	-	0.53	1.94E-05	1.46E-03
regulation of ion transmembrane transport (GO:0034765)	490	42	19.95	+	2.11	1.97E-05	1.47E-03
regulation of transcription by RNA polymerase II (GO:0006357)	2264	134	92.18	+	1.45	2.04E-05	1.52E-03
positive regulation of nucleic acid-templated transcription (GO:1903508)	1658	104	67.51	+	1.54	2.16E-05	1.60E-03
positive regulation of RNA biosynthetic process (GO:1902680)	1659	104	67.55	+	1.54	2.18E-05	1.61E-03
stem cell differentiation (GO:0048863)	158	20	6.43	+	3.11	2.30E-05	1.69E-03
striated muscle tissue development (GO:0014706)	287	29	11.69	+	2.48	2.35E-05	1.72E-03
adenylyl cyclase-modulating G protein-coupled receptor signaling pathway (GO:0007188)	215	24	8.75	+	2.74	2.45E-05	1.78E-03
cyclic-nucleotide-mediated signaling (GO:0019935)	173	21	7.04	+	2.98	2.56E-05	1.85E-03
cardiovascular system development (GO:0072358)	532	44	21.66	+	2.03	2.62E-05	1.89E-03
regulation of cell death (GO:0010941)	1706	106	69.46	+	1.53	2.72E-05	1.95E-03
skeletal system development (GO:0001501)	502	42	20.44	+	2.05	2.76E-05	1.98E-03
regulation of cellular component organization (GO:0051128)	2428	141	98.86	+	1.43	2.83E-05	2.01E-03
epithelium development (GO:0060429)	1121	76	45.64	+	1.67	3.07E-05	2.18E-03
inner ear development (GO:0048839)	204	23	8.31	+	2.77	3.11E-05	2.20E-03
positive regulation of cellular metabolic process (GO:0031325)	3405	186	138.64	+	1.34	3.28E-05	2.31E-03
regulation of axon guidance (GO:1902667)	43	10	1.75	+	5.71	3.37E-05	2.36E-03
regulation of axonogenesis (GO:0050770)	191	22	7.78	+	2.83	3.43E-05	2.39E-03
regulation of peptide hormone secretion (GO:0090276)	220	24	8.96	+	2.68	3.43E-05	2.38E-03
regulation of transmembrane transport (GO:0034762)	575	46	23.41	+	1.96	3.44E-05	2.38E-03
positive regulation of transcription by RNA polymerase II (GO:0045944)	1224	81	49.84	+	1.63	3.45E-05	2.37E-03
regulation of developmental growth (GO:0048638)	342	32	13.93	+	2.3	3.64E-05	2.49E-03
regulation of gliogenesis (GO:0014013)	124	17	5.05	+	3.37	3.78E-05	2.58E-03
ion transport (GO:0006811)	1342	87	54.64	+	1.59	3.84E-05	2.61E-03

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heart development (GO:0007507)	526	43	21.42	+	2.01	3.97E-05	2.69E-03
positive regulation of metabolic process (GO:0009893)	3716	200	151.31	+	1.32	4.01E-05	2.70E-03
axon guidance (GO:0007411)	265	27	10.79	+	2.5	4.22E-05	2.83E-03
eye morphogenesis (GO:0048592)	152	19	6.19	+	3.07	4.27E-05	2.85E-03
mRNA metabolic process (GO:0016071)	696	9	28.34	-	0.32	4.36E-05	2.90E-03
regulation of muscle organ development (GO:0048634)	139	18	5.66	+	3.18	4.45E-05	2.95E-03
ear morphogenesis (GO:0042471)	126	17	5.13	+	3.31	4.53E-05	2.99E-03
neuron projection guidance (GO:0097485)	268	27	10.91	+	2.47	4.80E-05	3.15E-03
negative regulation of axon guidance (GO:1902668)	27	8	1.1	+	7.28	4.88E-05	3.19E-03
response to auditory stimulus (GO:0010996)	27	8	1.1	+	7.28	4.88E-05	3.18E-03
positive regulation of response to stimulus (GO:0048584)	2458	141	100.08	+	1.41	4.98E-05	3.23E-03
cardiac chamber morphogenesis (GO:0003206)	128	17	5.21	+	3.26	5.41E-05	3.50E-03
regulation of neuron projection development (GO:0010975)	516	42	21.01	+	2	5.42E-05	3.49E-03
response to estradiol (GO:0032355)	143	18	5.82	+	3.09	6.21E-05	3.98E-03
intracellular signal transduction (GO:0035556)	1705	104	69.42	+	1.5	6.27E-05	4.00E-03
negative regulation of ion transport (GO:0043271)	157	19	6.39	+	2.97	6.34E-05	4.03E-03
adenylate cyclase-activating G protein-coupled receptor signaling pathway (GO:0007189)	130	17	5.29	+	3.21	6.44E-05	4.08E-03
anterior/posterior pattern specification (GO:0009952)	216	23	8.79	+	2.62	6.95E-05	4.38E-03
muscle tissue development (GO:0060537)	301	29	12.26	+	2.37	7.05E-05	4.43E-03
regulation of nitrogen compound metabolic process (GO:0051171)	5891	294	239.87	+	1.23	7.47E-05	4.68E-03
regulation of cation channel activity (GO:2001257)	188	21	7.65	+	2.74	7.65E-05	4.77E-03
inner ear morphogenesis (GO:0042472)	106	15	4.32	+	3.48	7.73E-05	4.80E-03
muscle contraction (GO:0006936)	246	25	10.02	+	2.5	8.72E-05	5.40E-03
multicellular organismal response to stress (GO:0033555)	71	12	2.89	+	4.15	8.96E-05	5.52E-03
vasculature development (GO:0001944)	522	42	21.25	+	1.98	9.25E-05	5.68E-03
regulation of membrane potential (GO:0042391)	441	37	17.96	+	2.06	1.01E-04	6.20E-03
regulation of cell morphogenesis involved in differentiation (GO:0010769)	313	29	12.74	+	2.28	1.02E-04	6.20E-03
regulation of primary metabolic process (GO:0080090)	6077	301	247.44	+	1.22	1.02E-04	6.18E-03

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response to external stimulus (GO:0009605)	2477	140	100.86	+	1.39	1.04E-04	6.29E-03
cell surface receptor signaling pathway (GO:0007166)	2493	141	101.51	+	1.39	1.08E-04	6.50E-03
blood vessel development (GO:0001568)	499	40	20.32	+	1.97	1.09E-04	6.54E-03
negative regulation of response to external stimulus (GO:0032102)	565	44	23.01	+	1.91	1.10E-04	6.55E-03
tissue morphogenesis (GO:0048729)	568	44	23.13	+	1.9	1.15E-04	6.87E-03
regulation of secretion by cell (GO:1903530)	783	56	31.88	+	1.76	1.17E-04	6.97E-03
protein complex oligomerization (GO:0051259)	235	24	9.57	+	2.51	1.19E-04	7.04E-03
sensory perception of chemical stimulus (GO:0007606)	540	6	21.99	-	0.27	1.21E-04	7.11E-03
positive regulation of blood circulation (GO:1903524)	74	12	3.01	+	3.98	1.27E-04	7.46E-03
regulation of ion transmembrane transporter activity (GO:0032412)	272	26	11.08	+	2.35	1.30E-04	7.61E-03
endocrine system development (GO:0035270)	125	16	5.09	+	3.14	1.31E-04	7.64E-03
positive regulation of cellular biosynthetic process (GO:0031328)	2027	118	82.53	+	1.43	1.31E-04	7.63E-03
spinal cord development (GO:0021510)	112	15	4.56	+	3.29	1.34E-04	7.78E-03
regulation of cellular metabolic process (GO:0031323)	6284	309	255.87	+	1.21	1.38E-04	7.95E-03
regulation of apoptotic process (GO:0042981)	1557	95	63.4	+	1.5	1.57E-04	8.99E-03
regulation of metabolic process (GO:0019222)	6772	329	275.74	+	1.19	1.62E-04	9.28E-03
positive regulation of RNA metabolic process (GO:0051254)	1748	104	71.17	+	1.46	1.63E-04	9.28E-03
negative regulation of gliogenesis (GO:0014014)	43	9	1.75	+	5.14	1.67E-04	9.48E-03
pituitary gland development (GO:0021983)	43	9	1.75	+	5.14	1.67E-04	9.45E-03
positive regulation of locomotion (GO:0040017)	562	43	22.88	+	1.88	1.68E-04	9.50E-03
skeletal system morphogenesis (GO:0048705)	244	24	9.94	+	2.42	1.71E-04	9.62E-03
tissue regeneration (GO:0042246)	65	11	2.65	+	4.16	1.73E-04	9.68E-03
cardiac chamber development (GO:0003205)	171	19	6.96	+	2.73	1.76E-04	9.81E-03
cell-cell adhesion (GO:0098609)	505	40	20.56	+	1.95	1.79E-04	9.95E-03
regulation of blood circulation (GO:1903522)	290	27	11.81	+	2.29	1.79E-04	9.93E-03
regulation of insulin secretion (GO:0050796)	186	20	7.57	+	2.64	1.79E-04	9.90E-03
positive regulation of biosynthetic process (GO:0009891)	2059	119	83.84	+	1.42	1.83E-04	1.01E-02
regulation of cell morphogenesis (GO:0022604)	512	40	20.85	+	1.92	2.01E-04	1.10E-02

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regulation of cytosolic calcium ion concentration (GO:0051480)	342	30	13.93	+	2.15	2.02E-04	1.10E-02
response to wounding (GO:0009611)	579	44	23.58	+	1.87	2.03E-04	1.10E-02
regulation of synaptic vesicle cycle (GO:0098693)	118	15	4.8	+	3.12	2.25E-04	1.22E-02
regulation of programmed cell death (GO:0043067)	1579	95	64.29	+	1.48	2.28E-04	1.23E-02
rhythmic behavior (GO:0007622)	26	7	1.06	+	6.61	2.40E-04	1.29E-02
regulation of macromolecule metabolic process (GO:0060255)	6215	304	253.06	+	1.2	2.42E-04	1.30E-02
regulation of cell projection organization (GO:0031344)	700	50	28.5	+	1.75	2.43E-04	1.30E-02
positive regulation of macromolecule biosynthetic process (GO:0010557)	1934	112	78.75	+	1.42	2.48E-04	1.32E-02
regulation of retinal ganglion cell axon guidance (GO:0090259)	5	4	0.2	+	19.65	2.50E-04	1.33E-02
epoxide metabolic process (GO:0097176)	5	4	0.2	+	19.65	2.50E-04	1.33E-02
regulation of transcription, DNA-templated (GO:0006355)	3469	183	141.25	+	1.3	2.58E-04	1.36E-02
regulation of transmembrane transporter activity (GO:0022898)	281	26	11.44	+	2.27	2.59E-04	1.36E-02
negative regulation of chemotaxis (GO:0050922)	57	10	2.32	+	4.31	2.62E-04	1.37E-02
negative regulation of cell motility (GO:2000146)	282	26	11.48	+	2.26	2.67E-04	1.40E-02
positive regulation of neuron differentiation (GO:0045666)	382	32	15.55	+	2.06	2.69E-04	1.40E-02
response to abiotic stimulus (GO:0009628)	1165	74	47.44	+	1.56	2.76E-04	1.43E-02
regulation of nucleic acid-templated transcription (GO:1903506)	3536	186	143.98	+	1.29	2.84E-04	1.47E-02
cAMP-mediated signaling (GO:0019933)	149	17	6.07	+	2.8	2.86E-04	1.48E-02
regulation of RNA biosynthetic process (GO:2001141)	3541	186	144.18	+	1.29	2.88E-04	1.48E-02
positive regulation of nucleobase-containing compound metabolic process (GO:0045935)	1914	111	77.93	+	1.42	2.90E-04	1.49E-02
regulation of striated muscle tissue development (GO:0016202)	135	16	5.5	+	2.91	2.90E-04	1.49E-02
cellular chemical homeostasis (GO:0055082)	762	53	31.03	+	1.71	2.99E-04	1.52E-02
inorganic ion homeostasis (GO:0098771)	726	51	29.56	+	1.73	3.11E-04	1.58E-02
ncRNA metabolic process (GO:0034660)	515	6	20.97	-	0.29	3.24E-04	1.64E-02
regulation of plasma membrane bounded cell projection organization (GO:0120035)	691	49	28.14	+	1.74	3.26E-04	1.65E-02
negative regulation of cell migration (GO:0030336)	267	25	10.87	+	2.3	3.27E-04	1.65E-02

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central nervous system neuron development (GO:0021954)	83	12	3.38	+	3.55	3.30E-04	1.66E-02
wound healing (GO:0042060)	485	38	19.75	+	1.92	3.31E-04	1.66E-02
export from cell (GO:0140352)	1049	68	42.71	+	1.59	3.33E-04	1.66E-02
negative regulation of axonogenesis (GO:0050771)	71	11	2.89	+	3.8	3.42E-04	1.70E-02
second-messenger-mediated signaling (GO:0019932)	339	29	13.8	+	2.1	3.49E-04	1.73E-02
negative regulation of neuron projection development (GO:0010977)	152	17	6.19	+	2.75	3.53E-04	1.74E-02
regulation of muscle tissue development (GO:1901861)	138	16	5.62	+	2.85	3.63E-04	1.79E-02
dendrite morphogenesis (GO:0048813)	60	10	2.44	+	4.09	3.77E-04	1.85E-02
negative regulation of multicellular organism growth (GO:0040015)	12	5	0.49	+	10.23	3.78E-04	1.85E-02
cellular homeostasis (GO:0019725)	924	61	37.62	+	1.62	3.86E-04	1.88E-02
cellular response to lipid (GO:0071396)	529	40	21.54	+	1.86	3.88E-04	1.89E-02
cation homeostasis (GO:0055080)	714	50	29.07	+	1.72	3.96E-04	1.92E-02
regulation of hormone secretion (GO:0046883)	274	25	11.16	+	2.24	3.99E-04	1.93E-02
regulation of transporter activity (GO:0032409)	293	26	11.93	+	2.18	4.00E-04	1.93E-02
positive regulation of catalytic activity (GO:0043085)	1477	89	60.14	+	1.48	4.09E-04	1.97E-02
outflow tract morphogenesis (GO:0003151)	73	11	2.97	+	3.7	4.23E-04	2.03E-02
morphogenesis of an epithelium (GO:0002009)	440	35	17.92	+	1.95	4.25E-04	2.03E-02
blood vessel morphogenesis (GO:0048514)	410	33	16.69	+	1.98	4.36E-04	2.08E-02
gliogenesis (GO:0042063)	230	22	9.37	+	2.35	4.36E-04	2.07E-02
negative regulation of cell morphogenesis involved in differentiation (GO:0010771)	99	13	4.03	+	3.22	4.38E-04	2.07E-02
rhythmic process (GO:0048511)	277	25	11.28	+	2.22	4.42E-04	2.09E-02
bone mineralization (GO:0030282)	50	9	2.04	+	4.42	4.47E-04	2.10E-02
regulation of growth (GO:0040008)	684	48	27.85	+	1.72	4.52E-04	2.12E-02
cardiac septum morphogenesis (GO:0060411)	74	11	3.01	+	3.65	4.68E-04	2.19E-02
response to steroid hormone (GO:0048545)	329	28	13.4	+	2.09	4.80E-04	2.24E-02
cognition (GO:0050890)	307	27	12.5	+	2.16	4.81E-04	2.24E-02
small molecule metabolic process (GO:0044281)	1718	100	69.95	+	1.43	4.91E-04	2.28E-02
cellular ion homeostasis (GO:0006873)	660	47	26.87	+	1.75	4.91E-04	2.27E-02
regulation of nucleobase-containing compound metabolic process (GO:0019219)	4065	208	165.52	+	1.26	4.95E-04	2.28E-02

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embryonic limb morphogenesis (GO:0030326)	128	15	5.21	+	2.88	4.95E-04	2.28E-02
embryonic appendage morphogenesis (GO:0035113)	128	15	5.21	+	2.88	4.95E-04	2.27E-02
regulation of animal organ morphogenesis (GO:2000027)	260	24	10.59	+	2.27	4.97E-04	2.27E-02
activation of adenylate cyclase activity (GO:0007190)	40	8	1.63	+	4.91	5.00E-04	2.28E-02
negative regulation of signal transduction (GO:0009968)	1284	79	52.28	+	1.51	5.00E-04	2.27E-02
porphyrin-containing compound metabolic process (GO:0006778)	51	9	2.08	+	4.33	5.08E-04	2.30E-02
intermediate filament-based process (GO:0045103)	51	9	2.08	+	4.33	5.08E-04	2.29E-02
epithelial tube morphogenesis (GO:0060562)	311	27	12.66	+	2.13	5.26E-04	2.37E-02
transmembrane receptor protein serine/threonine kinase signaling pathway (GO:0007178)	198	20	8.06	+	2.48	5.38E-04	2.42E-02
gene expression (GO:0010467)	2043	54	83.19	-	0.65	5.72E-04	2.56E-02
regulation of bone mineralization (GO:0030500)	76	11	3.09	+	3.55	5.73E-04	2.56E-02
metal ion homeostasis (GO:0055065)	634	45	25.81	+	1.74	5.73E-04	2.55E-02
skeletal muscle tissue development (GO:0007519)	130	15	5.29	+	2.83	5.73E-04	2.55E-02
smooth muscle contraction (GO:0006939)	52	9	2.12	+	4.25	5.75E-04	2.55E-02
feeding behavior (GO:0007631)	89	12	3.62	+	3.31	5.81E-04	2.57E-02
response to ketone (GO:1901654)	201	20	8.18	+	2.44	5.93E-04	2.62E-02
response to pain (GO:0048265)	31	7	1.26	+	5.55	5.98E-04	2.63E-02
positive regulation of cellular component movement (GO:0051272)	563	41	22.92	+	1.79	6.05E-04	2.65E-02
cellular response to toxic substance (GO:0097237)	220	21	8.96	+	2.34	6.08E-04	2.66E-02
enzyme linked receptor protein signaling pathway (GO:0007167)	726	50	29.56	+	1.69	6.19E-04	2.70E-02
camera-type eye development (GO:0043010)	317	27	12.91	+	2.09	6.21E-04	2.70E-02
regulation of mitochondrial depolarization (GO:0051900)	22	6	0.9	+	6.7	6.34E-04	2.75E-02
positive regulation of hydrolase activity (GO:0051345)	770	52	31.35	+	1.66	6.47E-04	2.80E-02
skeletal muscle cell differentiation (GO:0035914)	53	9	2.16	+	4.17	6.50E-04	2.80E-02
regeneration (GO:0031099)	162	17	6.6	+	2.58	6.85E-04	2.95E-02
regulation of RNA metabolic process (GO:0051252)	3807	195	155.01	+	1.26	7.01E-04	3.01E-02

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porphyrin-containing compound biosynthetic process (GO:0006779)	32	7	1.3	+	5.37	7.04E-04	3.01E-02
transport (GO:0006810)	4550	228	185.26	+	1.23	7.13E-04	3.04E-02
cellular response to BMP stimulus (GO:0071773)	105	13	4.28	+	3.04	7.24E-04	3.08E-02
response to BMP (GO:0071772)	105	13	4.28	+	3.04	7.24E-04	3.07E-02
positive regulation of cell motility (GO:2000147)	547	40	22.27	+	1.8	7.24E-04	3.07E-02
developmental growth involved in morphogenesis (GO:0060560)	119	14	4.85	+	2.89	7.27E-04	3.07E-02
regulation of muscle contraction (GO:0006937)	163	17	6.64	+	2.56	7.30E-04	3.07E-02
biological adhesion (GO:0022610)	930	60	37.87	+	1.58	7.52E-04	3.16E-02
regulation of voltage-gated calcium channel activity (GO:1901385)	43	8	1.75	+	4.57	7.60E-04	3.19E-02
connective tissue development (GO:0061448)	225	21	9.16	+	2.29	7.63E-04	3.19E-02
cellular response to prostaglandin stimulus (GO:0071379)	23	6	0.94	+	6.41	7.73E-04	3.22E-02
response to stress (GO:0006950)	3635	187	148.01	+	1.26	7.83E-04	3.25E-02
mRNA processing (GO:0006397)	477	6	19.42	-	0.31	7.91E-04	3.28E-02
regulation of gene expression (GO:0010468)	4494	225	182.98	+	1.23	7.91E-04	3.27E-02
gland development (GO:0048732)	421	33	17.14	+	1.93	8.01E-04	3.30E-02
cellular response to nutrient (GO:0031670)	67	10	2.73	+	3.67	8.15E-04	3.35E-02
response to ethanol (GO:0045471)	135	15	5.5	+	2.73	8.17E-04	3.35E-02
tetrapyrrole biosynthetic process (GO:0033014)	33	7	1.34	+	5.21	8.25E-04	3.38E-02
response to prostaglandin (GO:0034694)	33	7	1.34	+	5.21	8.25E-04	3.37E-02
postsynapse organization (GO:0099173)	93	12	3.79	+	3.17	8.26E-04	3.36E-02
regulation of integrin activation (GO:0033623)	15	5	0.61	+	8.19	8.60E-04	3.49E-02
negative regulation of glial cell proliferation (GO:0060253)	15	5	0.61	+	8.19	8.60E-04	3.48E-02
mechanosensory behavior (GO:0007638)	15	5	0.61	+	8.19	8.60E-04	3.48E-02
regulation of cardiac muscle cell proliferation (GO:0060043)	44	8	1.79	+	4.47	8.68E-04	3.50E-02
limb morphogenesis (GO:0035108)	151	16	6.15	+	2.6	8.86E-04	3.56E-02
appendage morphogenesis (GO:0035107)	151	16	6.15	+	2.6	8.86E-04	3.55E-02
neuron fate commitment (GO:0048663)	68	10	2.77	+	3.61	9.03E-04	3.61E-02
nucleic acid metabolic process (GO:0090304)	2303	64	93.77	-	0.68	9.05E-04	3.61E-02
cellular metal ion homeostasis (GO:0006875)	570	41	23.21	+	1.77	9.15E-04	3.64E-02
response to catecholamine (GO:0071869)	108	13	4.4	+	2.96	9.17E-04	3.64E-02

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response to monoamine (GO:0071867)	108	13	4.4	+	2.96	9.17E-04	3.63E-02
trabecula formation (GO:0060343)	24	6	0.98	+	6.14	9.35E-04	3.69E-02
phosphorus metabolic process (GO:0006793)	2177	120	88.64	+	1.35	9.43E-04	3.71E-02
neuron fate specification (GO:0048665)	34	7	1.38	+	5.06	9.62E-04	3.78E-02
regulation of inflammatory response (GO:0050727)	537	39	21.87	+	1.78	9.63E-04	3.78E-02
segmentation (GO:0035282)	95	12	3.87	+	3.1	9.77E-04	3.82E-02
response to nutrient levels (GO:0031667)	538	39	21.91	+	1.78	9.78E-04	3.82E-02
reproductive structure development (GO:0048608)	432	33	17.59	+	1.88	9.81E-04	3.82E-02
regulation of epithelial cell proliferation (GO:0050678)	343	28	13.97	+	2	9.85E-04	3.83E-02
lung morphogenesis (GO:0060425)	45	8	1.83	+	4.37	9.88E-04	3.83E-02
regulation of monooxygenase activity (GO:0032768)	57	9	2.32	+	3.88	1.03E-03	3.99E-02
positive regulation of blood vessel diameter (GO:0097755)	57	9	2.32	+	3.88	1.03E-03	3.98E-02
neuron migration (GO:0001764)	124	14	5.05	+	2.77	1.05E-03	4.02E-02
regulation of neurotransmitter secretion (GO:0046928)	110	13	4.48	+	2.9	1.07E-03	4.10E-02
skeletal muscle organ development (GO:0060538)	139	15	5.66	+	2.65	1.07E-03	4.10E-02
establishment of localization (GO:0051234)	4680	232	190.56	+	1.22	1.09E-03	4.16E-02
cardiac muscle tissue regeneration (GO:0061026)	3	3	0.12	+	24.56	1.09E-03	4.16E-02
neuromuscular process controlling posture (GO:0050884)	16	5	0.65	+	7.67	1.09E-03	4.15E-02
coronary vasculature morphogenesis (GO:0060977)	16	5	0.65	+	7.67	1.09E-03	4.14E-02
response to ATP (GO:0033198)	35	7	1.43	+	4.91	1.12E-03	4.22E-02
response to progesterone (GO:0032570)	46	8	1.87	+	4.27	1.12E-03	4.23E-02
coronary vasculature development (GO:0060976)	46	8	1.87	+	4.27	1.12E-03	4.22E-02
negative regulation of amine transport (GO:0051953)	25	6	1.02	+	5.89	1.12E-03	4.21E-02
negative regulation of axon extension involved in axon guidance (GO:0048843)	25	6	1.02	+	5.89	1.12E-03	4.20E-02
circadian behavior (GO:0048512)	25	6	1.02	+	5.89	1.12E-03	4.19E-02
response to prostaglandin E (GO:0034695)	25	6	1.02	+	5.89	1.12E-03	4.18E-02
glial cell differentiation (GO:0010001)	179	18	7.29	+	2.47	1.13E-03	4.22E-02
learning or memory (GO:0007611)	265	23	10.79	+	2.13	1.14E-03	4.22E-02

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cell differentiation in spinal cord (GO:0021515)	58	9	2.36	+	3.81	1.15E-03	4.26E-02
cardiac septum development (GO:0003279)	111	13	4.52	+	2.88	1.15E-03	4.26E-02
secretion (GO:0046903)	1119	69	45.56	+	1.51	1.16E-03	4.27E-02
muscle structure development (GO:0061061)	483	36	19.67	+	1.83	1.16E-03	4.28E-02
negative regulation of cell projection organization (GO:0031345)	181	18	7.37	+	2.44	1.20E-03	4.41E-02
regulation of synaptic transmission, glutamatergic (GO:0051966)	71	10	2.89	+	3.46	1.21E-03	4.44E-02
cell adhesion (GO:0007155)	924	59	37.62	+	1.57	1.29E-03	4.70E-02
response to purine-containing compound (GO:0014074)	157	16	6.39	+	2.5	1.29E-03	4.70E-02
regulation of cellular biosynthetic process (GO:0031326)	4217	211	171.71	+	1.23	1.30E-03	4.71E-02
response to organophosphorus (GO:0046683)	142	15	5.78	+	2.59	1.30E-03	4.72E-02
regulation of cytokine production (GO:0001817)	734	49	29.89	+	1.64	1.31E-03	4.73E-02
phosphate-containing compound metabolic process (GO:0006796)	2150	118	87.54	+	1.35	1.31E-03	4.75E-02
regulation of sprouting angiogenesis (GO:1903670)	72	10	2.93	+	3.41	1.33E-03	4.81E-02
adenylate cyclase-activating adrenergic receptor signaling pathway (GO:0071880)	26	6	1.06	+	5.67	1.34E-03	4.80E-02
cellular response to prostaglandin E stimulus (GO:0071380)	17	5	0.69	+	7.22	1.37E-03	4.91E-02
Analysis Type:	PANTHER Overrepresentation Test (Released 20200407)						
Annotation Version and Release Date:	GO Ontology database DOI: 10.5281/zenodo.3727280 Released 2020-03-23						
Analyzed List:	DeepMage_genes (Homo sapiens)						
Reference List:	Homo sapiens (all genes in database)						
Test Type:	FISHER						
Correction:	FDR						

Supplementary Table 4. DeepMAge outperformed both the 71 CpG and the 89 CpG clocks published by Hannum et al. in 2013. The baseline is defined as the mean age assignment.

GEO Accession	MAE, years				RMSE, years				N
	71 CpG	89 CpG	DeepMAge	Baseline	71 CpG	89 CpG	DeepMAge	Baseline	
GSE102177	3.87	7.59	1.98	2.22	4.56	8.03	2.23	2.63	36
GSE103911	16.31	31.25	7.43	8.24	20.44	33.99	9.16	10.66	65
GSE105123	4.4	16.53	2.32	1.14	5.78	17.1	2.87	1.34	107
GSE107459	5.7	19.46	2.23	3.63	7.09	20.51	2.79	4.38	127

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GSE107737	8.19	15.9	3.87	2.88	9.99	17.12	4.96	3.32	24
GSE112696	6.89	14.64	4.42	2.33	7.23	15.14	5.17	2.94	12
GSE34639	0.98	1	1.79	0.5	1.1	1.12	2.06	0.5	48
GSE59065	8.31	19.49	5.93	23.46	10.26	21.11	8.14	23.63	295
GSE61496	18.14	22.85	2.77	15.07	22.01	27.23	3.7	15.42	310
GSE87582	7.63	17.16	5.4	4.53	9.46	19.41	6.04	5.67	21
GSE87640	14.12	19.35	4.53	9.78	17.85	23.52	6.54	11.9	240
GSE98876	10.45	21.13	3.49	7.99	14.13	24.48	4.64	9.98	71
GSE99624	8.89	19.71	4.12	8.74	11.41	22.05	5.43	9.81	48
Total	11.05	19.54	3.97	18.62	15.12	22.96	5.75	21.35	1404

GEO = Gene Expression Omnibus; N = Number of samples in the corresponding GEO project; MAE = Mean absolute error; RMSE = Root mean square error.

Supplementary Table 5. Linear regression coefficients for the model produced by replicating Horvath's training protocol. Ranks are based on absolute coefficient value (higher importance features come first).

Rank	CpG_site	coefficient	Ran k	CpG_site	coefficient	Ran k	CpG_site	coefficient	Ran k	CpG_site	coefficient
1	cg21801378	0.983653	31	cg19885761	0.355402	61	cg05675373	0.237629	91	cg07845392	0.176361
2	cg02479575	0.939384	32	cg04836038	0.354184	62	cg16168311	-0.233731	92	cg19759064	-0.175474
3	cg00059225	0.816305	33	cg27015931	-0.348080	63	cg14918082	0.233498	93	cg05724065	-0.175079
4	cg22736354	0.793852	34	cg00630583	-0.342940	64	cg11017269	-0.232564	94	cg08668790	0.172569
5	cg01580888	0.681322	35	cg17861230	0.340669	65	cg04587910	-0.231216	95	cg23320649	-0.172294
6	cg06493994	0.582153	36	cg17471102	-0.337370	66	cg02840794	-0.229842	96	cg25713185	0.170709
7	cg19761273	-0.568068	37	cg09118625	0.332719	67	cg06836772	-0.223745	97	cg17706173	0.169717
8	cg27225570	-0.566827	38	cg13663218	-0.329015	68	cg20392764	0.220477	98	cg15957394	0.169437
9	(Intercept)	-0.549722	39	cg11299964	-0.328907	69	cg19357849	-0.216828	99	cg15804973	-0.168001
10	cg09809672	-0.532471	40	cg22580512	-0.326412	70	cg15297650	-0.216779	100	cg12422450	0.167622
11	cg00343092	-0.500909	41	cg13921352	0.320154	71	cg11296937	-0.215436	101	cg07158339	-0.166068
12	cg04474832	-0.463950	42	cg18328933	-0.318381	72	cg04564646	-0.210781	102	cg12340144	-0.165421
13	cg14915263	-0.461811	43	cg07850604	0.309722	73	cg12261786	-0.210380	103	cg02654291	0.160027
14	cg00503840	0.455829	44	cg23124451	-0.309382	74	cg18055007	0.208290	104	cg01459453	-0.157035
15	cg04528819	0.446599	45	cg21256649	-0.308976	75	cg07388493	-0.206733	105	cg05492845	-0.152588
16	cg25256723	-0.440934	46	cg08468689	-0.307241	76	cg00168942	-0.205629	106	cg04983977	0.151666
17	cg16785344	-0.422005	47	cg21296230	0.299826	77	cg22947000	-0.203777	107	cg18440048	0.150148
18	cg26005082	0.418708	48	cg20125091	0.291461	78	cg20692569	0.200028	108	cg11554937	0.146277
19	cg24170090	-0.409602	49	cg13975369	0.289659	79	cg06615861	-0.199849	109	cg01919208	0.145546
20	cg08888956	-0.408093	50	cg13494498	0.280318	80	cg12437239	0.197764	110	cg11007423	0.143615
21	cg08209133	0.406863	51	cg18815943	0.277910	81	cg18008766	0.189601	111	cg00451635	-0.131398
22	cg02228185	-0.406239	52	cg06885782	-0.276366	82	cg11465372	0.188791	112	cg18628483	-0.130806
23	cg27320127	0.404825	53	cg14754581	0.275500	83	cg25148589	0.187226	113	cg24127874	0.130118
24	cg13500819	0.390582	54	cg11668844	0.264290	84	cg12467090	0.185320	114	cg26842024	0.128317
25	cg01511567	-0.390299	55	cg19945840	0.260856	85	cg15798153	0.184923	115	cg10822172	-0.128046
26	cg19722847	-0.387929	56	cg27544190	-0.258460	86	cg15836394	-0.183558	116	cg19046959	-0.125864
27	cg22809047	0.371073	57	cg14732136	-0.254872	87	cg17291001	0.182513	117	cg03330058	-0.125722
28	cg07408456	-0.362516	58	cg26614073	-0.253922	88	cg13899108	0.181476	118	cg26847866	-0.124492

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29	cg20295671	-0.361302	59	cg01007201	0.246585	89	cg10523019	0.179182	119	cg19560758	0.124417
30	cg01820374	-0.355981	60	cg18236477	0.244505	90	cg21232015	0.178062	120	cg09706243	-0.124360
Rank	CpG_site	coefficient									
121	cg13460409	0.120700	151	cg20761322	0.098329	181	cg24231716	0.073321	211	cg15410903	-0.052966
122	cg16363586	-0.119329	152	cg23749046	0.096361	182	cg02085507	0.072851	212	cg19904653	0.052474
123	cg17465304	0.118849	153	cg20240860	-0.094244	183	cg27210390	-0.072419	213	cg16714091	0.052409
124	cg02142461	0.118652	154	cg18691434	0.093386	184	cg20732137	0.072384	214	cg20419410	-0.052102
125	cg05671018	0.116750	155	cg25771195	0.092643	185	cg11051139	-0.070007	215	cg06288351	-0.052079
126	cg00433406	0.116722	156	cg27491887	0.092029	186	cg20143092	-0.066992	216	cg10648908	-0.051900
127	cg12024906	0.116126	157	cg23674788	0.089757	187	cg02196655	0.066945	217	cg23968383	0.051490
128	cg11896923	-0.115847	158	cg09238598	-0.089702	188	cg04425624	-0.065455	218	cg00563932	-0.050910
129	cg09667582	0.115700	159	cg00528967	-0.088380	189	cg16034652	0.064228	219	cg10681065	0.050569
130	cg14360917	0.115690	160	cg13697378	0.087401	190	cg08072716	0.064033	220	cg21432842	-0.050569
131	cg25762706	0.113164	161	cg15201877	0.086424	191	cg25020850	0.063756	221	cg05436231	0.050171
132	cg15538427	-0.112250	162	cg26203861	-0.085473	192	cg22971191	0.063552	222	cg15792367	-0.049766
133	cg17628717	0.111783	163	cg08317263	-0.085192	193	cg06238491	-0.063003	223	cg16529592	0.048889
134	cg15095327	0.111534	164	cg00689340	-0.083082	194	cg11618577	0.062549	224	cg02828104	-0.048105
135	cg16547529	0.111106	165	cg12782180	0.082635	195	cg26372517	0.062243	225	cg16330965	0.047424
136	cg09462576	-0.109677	166	cg15156836	-0.082545	196	cg18081258	-0.061605	226	cg17191178	0.047321
137	cg15013019	-0.108504	167	cg26673195	-0.082272	197	cg15563382	0.060942	227	cg11879514	0.046374
138	cg00240880	0.106645	168	cg02844545	0.081288	198	cg00187380	-0.060720	228	cg10322876	0.046245
139	cg16744741	-0.106124	169	cg23894058	0.080975	199	cg08032971	0.059374	229	cg25372195	0.045917
140	cg25459323	-0.105747	170	cg17655614	0.079729	200	cg02310296	0.058791	230	cg20969242	0.045905
141	cg19724470	-0.104476	171	cg22909609	-0.079372	201	cg23887396	-0.057687	231	cg13493001	0.045881
142	cg18303397	-0.103026	172	cg11393848	-0.078721	202	cg01600189	-0.056979	232	cg12830694	0.045029
143	cg26083396	-0.102282	173	cg10989517	0.077383	203	cg14709524	0.056268	233	cg03991512	-0.044471
144	cg12167564	0.102049	174	cg23303074	-0.076855	204	cg21426387	-0.056218	234	cg26845300	0.043818
145	cg07211259	-0.100932	175	cg11126134	0.076425	205	cg26394940	-0.055434	235	cg22472290	0.042385
146	cg00757070	-0.100919	176	cg21600563	-0.076349	206	cg20582779	0.055430	236	cg05358404	0.042356
147	cg19850406	0.100517	177	cg27016307	-0.075887	207	cg12289045	0.055241	237	cg08965235	-0.041639
148	cg24081819	-0.100099	178	cg13813391	0.075797	208	cg11819637	0.054954	238	cg10674793	0.041490
149	cg05749577	-0.099570	179	cg24847163	-0.075789	209	cg02489552	0.053384	239	cg10676060	0.041424
150	cg16913124	0.099268	180	cg09307279	-0.075082	210	cg19777783	0.053383	240	cg03019000	-0.041335
Rank	CpG_site	coefficient									
241	cg03929796	-0.041099	271	cg04304130	0.025783	301	cg19356189	-0.013159	331	cg03805684	0.004344
242	cg14166009	0.040661	272	cg23854009	0.025638	302	cg09195271	0.012800	332	cg26376809	-0.004212
243	cg22022041	0.040321	273	cg06736444	0.025217	303	cg02829654	0.012382	333	cg20436912	0.003965
244	cg06458239	0.039813	274	cg23881601	-0.025032	304	cg05294243	0.012290	334	cg06144905	0.003305
245	cg21289015	0.039448	275	cg20648149	0.024993	305	cg27169020	0.012111	335	cg21098323	0.002805
246	cg08090640	-0.038989	276	cg03943081	0.024911	306	cg18847227	0.011814	336	cg20775254	0.002624
247	cg15408407	-0.038133	277	cg12774845	-0.024566	307	cg22335340	-0.011134	337	cg07895149	-0.002459
248	cg18017908	-0.037211	278	cg13269407	-0.024451	308	cg21301148	-0.010720	338	cg05507459	-0.002235
249	cg11219178	-0.036830	279	cg15537850	-0.024411	309	cg26057752	0.010613	339	cg20747455	0.002161
250	cg06896207	0.036030	280	cg22799321	0.023824	310	cg21448423	-0.010174	340	cg09554443	0.002072

SUPPLEMENTARY DATA

251	cg20492912	0.036028	281	cg25282410	0.023754	311	cg12426141	-0.010024	341	cg10281002	0.001749
252	cg22941086	0.035732	282	cg08558340	0.023500	312	cg20387706	0.009523	342	cg16519742	0.001362
253	cg06268694	0.035268	283	cg04123409	-0.022247	313	cg03224418	-0.008908	343	cg21652958	0.001228
254	cg25004981	0.033099	284	cg11976790	0.020600	314	cg18279742	0.008791	344	cg08723608	0.000896
255	cg10919204	0.032924	285	cg19109050	0.019781	315	cg08861115	0.008731	345	cg11377136	0.000827
256	cg26538442	0.032287	286	cg16858125	0.018828	316	cg10249734	0.008316	346	cg00208830	0.000789
257	cg15780361	0.031666	287	cg01560871	-0.016904	317	cg10917602	-0.008023	347	cg08124399	0.000608
258	cg06630241	0.031412	288	cg12717203	-0.016663	318	cg10362475	0.007987	348	cg07549715	0.000344
259	cg08331960	-0.030947	289	cg08022502	-0.016501	319	cg14972143	0.007970			
260	cg21057046	-0.030385	290	cg16254309	0.016370	320	cg05113558	0.007859			
261	cg25221254	0.029982	291	cg04633513	0.016306	321	cg18902090	0.007801			
262	cg04765422	0.029879	292	cg25809905	-0.015482	322	cg00308665	-0.007369			
263	cg06971096	0.029082	293	cg24341129	0.015423	323	cg15379633	0.007226			
264	cg18678185	-0.028961	294	cg21663431	-0.015366	324	cg05420896	0.006647			
265	cg26976437	0.028689	295	cg25564800	-0.014755	325	cg13726191	-0.006321			
266	cg22215728	0.028028	296	cg01656853	0.014466	326	cg00565075	0.005736			
267	cg22805308	0.027331	297	cg13302154	-0.014253	327	cg19595170	-0.005258			
268	cg26297688	0.027140	298	cg01400401	0.014041	328	cg14576824	0.005170			
269	cg08822227	-0.027097	299	cg22511947	0.013973	329	cg01753375	-0.004934			
270	cg17832674	-0.026777	300	cg17453778	0.013909	330	cg09150232	-0.004447			